# RADAM Conference 2005

17th-20th March 2005, Potsdam near Berlin, Germany

## Radiation Damage in Biomolecular Systems

Conference within the COST P9 Action
supported by the European Science Foundation

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## Conference site

Seminaris SeeHotel Potsdam
An der Pirschheide 40
14471 Potsdam
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## Host Institution

Hahn-Meitner Institut
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# Preface

The COST Action RADAM (RADiation DAMage) was established by the COST Physics Committee as its ninth Action Programme (P9) in 2002. Funded for 4 years it was initially ratified by 14 European countries and was formally launched in November 2003. In the first 18 months the Action has arranged over 50 short visits involving over 30 research groups, supported 7 conferences and the number of the European countries formally joining the action has increased to 19. The main objective of the RADAM project is to obtain a detailed understanding of the fundamental interaction processes initiated by the deposition of various types of radiation in biological material. This also introduces the exciting prospect that it may be possible to manipulate the effects of ionizing radiation at a molecular level within the cell.

The Action is subdivided into 5 Working Groups each of which is devoted to a specific field. Thus, a wide range of complementary experimental and theoretical expertise is brought together under this Programme. The research requires an interdisciplinary approach to the interaction of photons, ions and electrons with bio-molecular systems. The elucidation of fundamental energy transfer and coupling mechanisms, ionization, charge transport, and reaction behaviour will in turn be used to develop models of track structures in irradiated media. Such models can be used to determine a more reliable quantification of human epidemiological experience when subject to low radiation doses.

The participants of the Action meet annually to discuss the progress of their common research work. The first Annual Workshop was held in Lyon from June 24$^{th}$ to 27$^{th}$, 2004. The scientific programme of the Workshop in Lyon was structured by the individual Working Groups, which organized excellent talks devoted to their specialized topics. During the meeting of the Management Committee it was agreed that at the next Annual Workshop it would be preferable to provide time to Tutorial Speakers that can enhance the connections between the different Working Groups.

In 2005 the Annual Workshop of the COST Action RADAM takes place at Potsdam from March 16$^{th}$ to 20$^{th}$. The conference site is the Seminaris SeeHotel, which is well known for successfully hosting workshops and conferences. In accordance with the recommendation of the Management Committee, the programme is structured so that about half the time is devoted to Tutorial Speakers, whereas the other half is devoted to specialized topics. To enhance the interdisciplinary connections, contributions from different Working Groups are mixed in some Sessions.

We wish you all a joyful conference communicating physics and finding new friends !

Nigel Mason
Chairman of the COST Action P9

Nikolaus Stolterfoht
Local Chairman of the RADAM05

# Programme of RADAM05

## Wednesday, March 16

Afternoon: Arrival and Registration

19:00 **Dinner**

## Thursday, March 17

08:00 Breakfast

09:00 **Nico Stolterfoht** and **Nigel Mason**, (30)
*Opening*

**Chair**: Nico Stolterfoht

09:30 **Franco Gianturco** (T,40), CASPUR, Roma, Italy
*Modelling transient negative ion formations in gas-phase biosystems*

10:10 Coffee Pause (30)

**Chair:** Kevin McGuigan

10:40 **Melvyn Folkard** (T,30), Gray Cancer Institute, Northwood, UK
*Ionizing radiation track structure and DNA damage*

11:10 **Paul Scheier** (T,30), Universität Insbruck, Austria
*The use of isotope and site labelling for the identification of DEA peaks in biomolecules*

11:40 **Lars Andersen** (25), University of Aarhus, Denmark
*Photo-absorption measurements of protein chromophores in vacuo*

12.05 Session End

12:15 Lunch and free time

**Chair:** David Field

14:00 **Emilie Cauët** (20), Université Libre de Bruxelles, Belgium
*Ab initio calculation of the potential energy surfaces describing electron transfer in a stack dimer of DNA bases*

14:20 **John Sabin** (20), University of Odense, Denmark
*Ion-biomolecule collisions: Fragmentation products and cross Sections*

14:40 **Przemek Sobocinski** (20), Hahn-Meitner-Institut, Berlin, Germany
*Absolute cross sections for the fragmentation of water molecules in collisions with slow $He^{2+}$ ions*

15:00 **Sandrine Lacombe** (20), Université Paris Sud, Orsay, France
*Ion irradiation of DNA*

15:20 Coffee Pause (30)

**Chair:** Bratislav Marinkovic

15:50 **Yann A. Gauduel** (T,30), Ecole Polytechnique Palaiseau, Paris, France
*Low and high energy radiation femtochemistry of biological interest*

16.20 **Sylwia Ptasinska** (20), Universität Innsbruck, Austria
*Low energy electron interactions with porphine derivates*

16.40 **Gustavo Garcia** (25), CSIC, Madrid, Spain
*Energy deposition model at molecular level in tissue equivalent materials*

**Chair:** Ronnie Hoekstra

17.05 **Poster Introduction**

18:15 Session End

19:00 Dinner

20:00 Poster Session

## Friday, March 18

8:00 Breakfast

**Chair**: Eugen Illenberger

9:00 **Wolfgang Domcke** (T,40), Technische Universität München, Germany
*Conical intersections of potential-energy surfaces and ultra fast deactivation of excited electronic states*

9:40 **Herwig Paretzke** (T,40), Institut für Strahlenschutz, Neuherberg, Germany
*Which radiation track structure properties couple physics interactions to biology effects*

10:20 Coffee Pause (30)

**Chair** : Marie-Christine Bacchus

10:50 **Evelyne Sage** (T,35), Institute Curie, Paris, France
*DNA damage, repair and mutagenesis*

11:25 **Kevin Prise** (T,35), Gray Cancer Institute, Northwood, UK
*Radiation-induced bystander responses*

12.00 Session End

12:15 Lunch and free time

14:00 **Excursion to Potsdam**

18:00 End of Excursion

19:00 Dinner

20:00 Poster Session

## Saturday, March 19

8:00 Breakfast

**Chair**: Michel Farizon

9:00 **Bojidar Galutzov** (T,35), Sofia University, Sofia, Bulgaria
*Supramolecular and subcellular effects of ionizing radiation*

9:35 **Melanie Spotheim-Maurizot** (T,35), CBM, Orleans, France
*Radiolysis of DNA binding proteins and functional consequences*

10:10 **Viktorie Stisova** (20), Nuclear Physics Institute, Prague, Czech Republic
*Effect of estrogen receptor on radiation-induced damage to DNA*

10:30 Coffee Pause (30)

**Chair:** Rita Plukiene

11.00 **Preben Hvelplund** (T,40), University of Aarhus, Denmark
*Biomolecular ions in accelerators and storage rings*

11:40 **Thomas Schlathölter** (20), KVI, Groningen, The Netherlands
*Ion induced fragmentation of DNA building blocks: isolated molecules and clusters*

12.00 Session End

12:15 Lunch and free Time

**Chair:** Belá Sulik

14:00 **Henrik Cederquist** (T, 35), Stockholm University, Stockhom, Sweden
*Sources traps and rings which can be used for radiation damage experiments at the molecular level*

14:35 **Bernd Huber (T,35)**, CIRIL, Caen, France
*Ion-induced fragmentation and aggregation of small biomolecular systems*

15:10 **Berndt Grosswendt** (T,35), PTB, Braunschweig, Germany
*Basic quantities in radiation physics including track structures*

15:45 **Stanislaw Pszona** (25), Soltan Institute, Otwok/Swierk, Poland
*Microdosimetric measurements of track structure quantities*

16:10 Coffee Pause (30)

**Chair:** Nigel Mason

16:40 **Werner Friedland** (25), GSF, Neuherberg, Germany
*Microscopic target structures in the biophysical simulation of radiation effects in cells*

17:05 **Andrea Ottolenghi** (25), Università degli Studi di Pavia, Italy
*Modelling the evolution of radiobiological damage with focus on target structures*

17:30 **Clemens von Sonntag** (20), MPI
*Free radical DNA damage and repair - a chemical perspective*

17:50 **Herwig Paretzke,** Institut für Strahlenschutz, Neuherberg, Germany
*Final Remarks and good bye*

18:10 Session End

19:00 - 20:00 Dinner

## Sunday, March 20

8:00 Breakfast

9:00 -11:00 Committee meeting

Good bye and departure

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Tutorial contributions are denoted T, numbers in parenthesis are in minutes

# Abstracts

## Invited Talks

# Modelling transient negative ion formations in gas-phase biosystems

F.A. Gianturco

Department of Chemistry, The University of Rome "La Sapienza",
Piazzale A. Moro 5, 00185 Rome, Italy

It has been firmly established by several experimental groups over the years that low-energy electrons are produced in large quantities when many types of materials are irradiated by high-energy radiation or by energetic particles, either charged or neutral. In the case of biological environments such electrons can further interact with the biomolecules causing the formation of a broad variety of highly reactive species in the form of either radicals or ions or both. The results of such processes are generally described as radiation damage.

Because of the general complexity of the biomolecules involved, it becomes very difficult for theory to realistically describe such different pathways of destructive damage at the molecular level. In the present seminar I shall try to outline a novel adiabatic modelling of the trapped, metastable electrons that has been carried out by our group in Rome over the last year or so [1-4], whereby specific suggestions can be made from calculations on the spatial shapes and features of the resonant compounds formed during the electron attachment. Such specific features can therefore be employed to assign different "precursors" to many of the fragmentation products observed experimentally from gas-phase data.

[1] F.A. Gianturco and R.R. Lucchese, *J. Chem. Phys.* **120**, (2004) 7446
[2] A Grandi, F.A. Gianturco and N. Sanna, *Phys. Rev. Lett.* **93**, (2004) 048103
[3] F.A. Gianturco and R.R. Lucchese, *J. Phys. Chem. A*, **108**, (2004) 7056
[4] F.A. Gianturco and R.R. Lucchese, *New Journal of Physics*, **6**, (2004) 66

# Ionizing radiation track structure and DNA damage

M. Folkard

Gray Cancer Institute, PO Box 100, Mount Vernon Hospital, Northwood, Middlesex, HA62JR, UK

It is well known that ionizing radiation damages living cells and tissues, a useful property that can be used to treat many forms of cancer (radiotherapy). However at some doses, ionizing radiation can cause cancer by inducing mutations and transformations with cells as a result of damage to the DNA. An important class of radiation-induced DNA damage is 'strand breaks' where a bond break occurs in the 'backbone' of either or both of the DNA helices. In particular, the double-strand break (DSB) where both strands are broken within a few base pairs of each other is known to be of critical importance; a single mis-repaired, or un-repaired DSB can lead to mutation, or cell death. The likelihood that a DSB will lead to irreversible cellular damage critically depends on the quality of the strand-break, which in turn, depends on the pattern and quantity of ionizations that occur in a section of the DNA helix. Penetrating radiations (i.e. energetic photons or electrons) are sparsely ionising, and therefore produce predominantly 'simple' breaks that are easily repaired. By contrast, energetic ions produce an abundance of clustered ionizations along the path of the particle track, caused both by the ions themselves and by low-energy secondary electrons. Such clusters can induce 'complex' strand-breaks in DNA, which are less easily repaired. Even sparsely ionising radiations produce some complex damage, primarily through the action of nanometre-sized clusters of ionisations at the low-energy track-ends of secondary electrons. The low-energy electrons produced by all radiations therefore have an important role in determining overall radiobiological effect.

A number of experimental strategies are being used to evaluate the 'energetics' of DNA damage by low-energy radiations. For example, experiments have been performed to quantify the amount of energy involved in the induction of strand-breaks in DNA. The approach used is to expose DNA to low-energy ionizing radiation at a range of energies and look for thresholds, below which single-strand and double-strand breaks are not produced. The target molecule for these studies is frequently extracted and purified plasmid DNA, which assumes a different topology depending on the damage it receives. The different forms of DNA can be readily quantified by gel electrophoresis, such that it is possible to measure the fraction of induced single-strand breaks (SSB) and DSB. It is observed that single- and double-strand breaks are readily induced in DNA by photons and electrons with energies as low as 6-7 eV. Further studies have shown electrons as low as a 0-4 eV can induce SSB. The observation that such effects occur at energies well below ionization thresholds means that mechanisms other than direct or indirect ionisation are important in producing observable biological effects. The damage that arises at these very low energies is thought to be due to rapid decays of transient molecular resonances localized on the DNA molecule. Consequently, important studies are now underway to understand both ionizing and non-ionizing pathways for radiation-induced DNA damage.

# The use of isotope and site labeling for the identification of DEA peaks in biomolecules

S. Ptasińska, S. Denifl, E. Illenberger[a], T.D. Märk and P. Scheier

Institut für Ionenphysik, Leopold-Franzens Universität Innsbruck and Center for Molecular Biosciences Innsbruck (CMBI), Technikerstr. 25, A-6020 Innsbruck, Austria
[a]Institut für Chemie - Physikalische und Theoretische Chemie, Freie Universität Berlin, Takustrasse 3, D-14195 Berlin, Germany

Free electron attachment to gas phase thymine leads exclusively to the formation of fragment anions. In the electron energy range between 1 and 3 eV the attachment cross section of the most dominant product (T-H) reveals several narrow resonances [1] (Fig. 1a). By using partially deuterated thymine where deuterium replaces all hydrogen atoms connected to carbon atoms it is possible to show that all these resonances originate from the abstraction of hydrogen from the two nitrogen sites [2]. However, in DNA one of these hydrogen atoms is missing where thymine is connected to the sugar and the other hydrogen atom is part of a hydrogen bridge to adenine. Attachment cross sections for the H abstraction from thymidine (thymine connected to deoxyribose) and 1-methyl-thymine show a single asymmetric resonance at about 2 eV (Fig. 1a) and thus demonstrate that for gas phase thymine the low energy resonances up to 2eV can be related to the H loss from the N1 position. The complementary reaction channel to the (T-H) formation, i.e. the H abstraction reveals a broad and structured feature in the energy range between 5 and 12 eV (Fig. 1b). By using partly deuterated thymine it can be shown that the different peaks in the H ion yield can unambiguously be associated to abstraction from the different molecular sites [3]. The energy dependence for H abstraction from the carbon sites shows a remarkable resemblance to the energy dependence of strand breaks observed in plasmid DNA suggesting that this reaction may be an important initial step towards strand breaks [4].

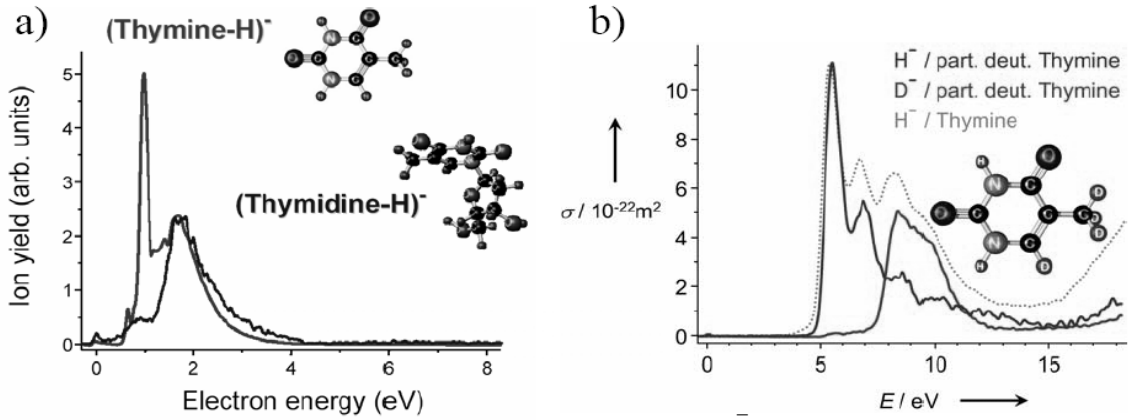



Fig 1: a) Ion efficiency curves for the formation of (M-H) via free electron attachment to thymine and thymidine. b) Attachment cross section for the H /D formation.

[1] S. Denifl, S.Ptasinska, M. Probst, J. Hrusak, P. Scheier and T.D. Märk, *J. Phys. Chem. A* **108** (2004) 6562
[2] H. Abdoul-Carime, S. Gohlke and E. Illenberger, *Phys. Rev. Lett.* **92** (2004) 168103
[3] S. Ptasińska, S. Denifl, T. D. Märk, P. Scheier, S. Gohlke, M. A. Huels and E. Illenberger, *Angew. Chem. Int. Ed.* (2005) in print
[4] B. Boudaiffa, P. Cloutier, D. Hunting, M. Huels and L. Sanche, *Science* **278** (2000) 1658

# Photo-absorption measurements of protein chromophores *in vacuo*.

Lars H Andersen

Department of Physics and Astronomy University of Aarhus, 8000 Aarhus C, Denmark

The electronic energy levels of molecules depend critically on the environment in which the molecules are located, and the colour of molecules (for example in a liquid) is thus sensitive to interactions with environments. This may be explored by electronic spectroscopy methods to achieve information on molecular interactions deep inside complex systems like proteins. The electronic perturbations may in certain proteins be large and cause significant shifts on the absorption wavelength. In other cases, proteins effectively shield their light-absorbing molecules from perturbations and the absorption conditions resemble those in vacuum. To be on firm ground when comparing electronic energies in different environments and for the sake of reference for molecular theory it is necessary to study the completely naked molecule (i.e. in vacuum). We have developed a technique at the electrostatic storage ring ELISA in Aarhus, where we studied bare chromophore ions from proteins like the Green Fluorescent Proteins (GFP) [1-5] and the Photoactive Yellow Protein (PYP) [6].

Perturbations on chromophores form the basis of colour tuning in visual pigments, where the chromophore is retinal in the protonated Schiff-base form. To understand the delicate perturbations that tune the absorption of vision proteins, comparisons have until now been made with the absorption of the chromophore in methanol. We show that the absorption maximum of retinal solvated in methanol is very different from that of the isolated chromophore [7]. Protein interactions responsible for colour tuning are causing a significant blue shift of the chromophore absorption instead of the red shift which has been assumed for decades.

[1] S. B. Nielsen *et al.*, *Phys. Rev. Lett.* **87** 2281021 (2001)
[2] L. H. Andersen *et al.*, *Nucl. Phys. Review*, **19** 176 (2002)
[3] L.H. Andersen, S.B. Nielsen and S.U. Pedersen, *Eur. Phys. J. D.,* **20** 597-600 (2002)
[4] S. Boye, *et al., Phys. Rev. Lett*. **90** 118103-1 (2003)
[5] S. Boyé *et al*., *J. Chem. Phys* **119**, 338-345 (2003)
[6] I.B. Nielsen *et al.* To be submitted
[7] L. H. Andersen, *et al*. Submitted

# Ab initio calculation of the potential energy surfaces describing electron transfer in a stack dimer of DNA bases

E. Cauët and J. Liévin

Service de Chimie Quantique et Photophysique, CP160/09 Université Libre de Bruxelles, 50 Avenue F. D. Roosevelt, B-1050 Brussels, Belgium

Electron abstraction from DNA bases plays an important role in biological processes like charge transport within double helical DNA and radiation damage to DNA. In this work, we have investigated with *ab initio* methods elementary steps related to such processes. We first present results on the ionization of isolated DNA bases and then on the electron migration from one base to another in a stacked dimer. These calculations imply the investigation of the ground and first excited states of the cations and imply the use of adapted methods of calculations, as discussed in another poster.

In the case of the isolated DNA bases, we obtain accurate values of the vertical and adiabatic ionization potentials. The excited states of the corresponding radical cations, which could contribute to some of the reactive processes of interest, are characterized for the first time. The ground state is found to be connected to the first excited state by a conical intersection, in all of the DNA bases. The topology of the corresponding potential energy surfaces has been characterized.

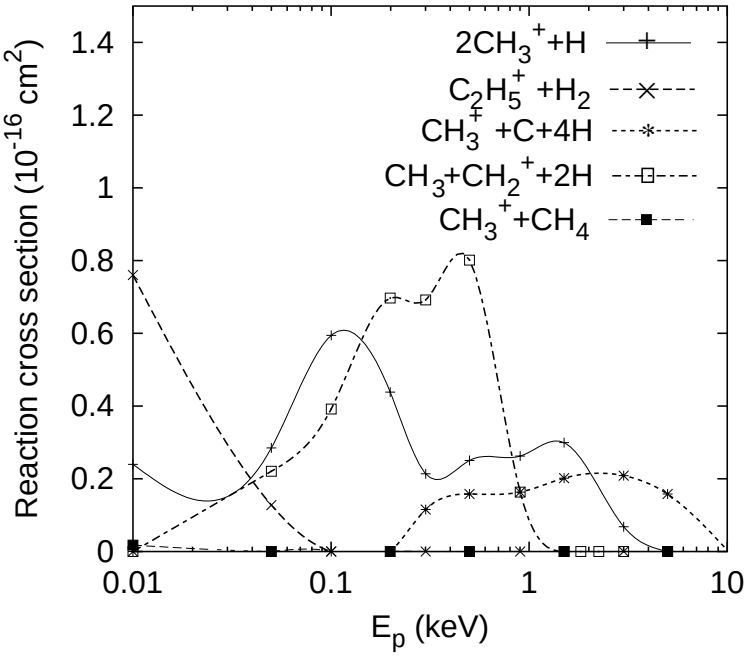
In the case of stacked pairs of DNA bases, we are focusing on an ionized Guanine-Guanine stack. We demonstrate that the electron migration from one Guanine to the other is governed by an avoided crossing occuring between the ground and the first excited states of the cation dimer. Cuts in the corresponding potential energy surfaces have been obtained by means of the CASSCF, CASPT2 and MRCI methods in order to localize the relevant geometrical parameters describing the electron transfer. Geometry optimizations are in progress for locating the stationary points along the reaction path.

# Ion-Biomolecule Collisions: Fragmentation Products & Cross Sections

John R. Sabin

Department of Physics, University of Florida and Department of Chemistry, University of Southern Denmark

In this presentation, I will introduce a theoretical scheme for studying the interaction of fast ions, electrons, and photons with molecules. Although the molecules under consideration are not, perhaps, of the size to make a biologist (or even a biochemist!) feel quite at home, they are the beginnings of a theoretical program to study the details of the interactions of particles with molecules of biological significance. The examples, such as the fragmentation cross section for various channels for protons impinging on ethane, will be illustrative of what we hope we will be able to do with real bio-molecules in time. In particular, I will look at collision and fragmentation cross sections, which are necessary for the understanding of the details of ion-molecule processes. The details of the formalism will be minimal.




Collaborators: Remigio Trujillo, Erik Deumens & Yngve Öhrn

# Absolute cross sections for the fragmentation of $H_2O$ molecules in collisions with slow $He^{2+}$ ions

P. Sobocinski[a], Z.D. Pešić[a], R. Hellhammer[a], J.-Y. Chesnel[b], B. Sulik[c], and N. Stolterfoht[a]

[a]Hahn-Meitner Institut, Glienickerstraße 100, D-14109 Berlin, Geramany
[b]CIRIL, Unité Mixte CEA-CNRS-EnsiCaen-Université de Caen Basse-Normandie
F-14050 Caen cedex 04, France
[c]Institute of Nuclear Research – ATOMKI, H-4001 Debrecen, Hungary

In this work, we investigate the ion-induced fragmentation of $H_2O$ molecules. The experiments were performed using $He^{2+}$ ions produced by the 14.5-GHz Electron Cyclotron Resonance (ECR) ion source facility at the Ionenstrahllabor (ISL) in Hahn-Meitner Institut, Berlin [1]. The energy of the projectile was varied from 1 to 5 keV. The experimental chamber, with a base pressure of $\sim 10^{-6}$ mbar, contains an electrostatic parallel-plate spectrometer, which can be rotated from $18^o$ to $135^o$ with respect to the incident ion beam direction. Similar work concerning collisions of $He^{2+}$ on $H_2O$ has been performed using the technique of translational energy spectroscopy [2].

As recently observed in the $Ne^{q+}$ + $H_2O$ collisions [3], two groups of peaks are clearly visible. The first one, which extends up to ~ 30 eV, corresponds to CE of the ionised target $(H_2O)^{q+}$ following electron capture at relatively large impact parameters. At higher energies, a second group corresponds to $H^+$, $O^+$ and $O^{2+}$ ions produced by binary collisions. In addition, the scattered projectiles $He^+$ and $He^{2+}$ have been detected. Absolute cross sections $d\sigma/d\Omega$, differential in the observation angle, were determined for the detection of all these species. In the analysis, particular attention was paid to the energetic fragments and scattered projectiles. In this case, our absolute cross sections are lower than those predicted by the Rutherford formula. Rather, our experimental values are in good agreement with absolute cross sections calculated by assuming an electronic screening function proposed by Ziegler *et al* [4]. The agreement between experimental and calculated cross sections shows that the ZBL screening function is an appropriate tool to predict absolute cross sections characterizing collisions between neutral targets and ions with velocities > 0.1 a.u.

[1] Grether M, Spieler A, Niemann D and Stolterfoht N. *Phys. Rev*. A **56**, 3794 (1997)
[2] Abu-Haija O, Kamber E Y and Ferguson S M, *Nucl. Instr. Methods in Phys. Res. B*. **205**, 634 (2003)
[3] Pešić Z D, Chesnel J-Y, Hellhammer R, Sulik B and Stolterfoht N *J. Phys. B. At. Mol. Opt. Phys*. **37**, 1405-1417 (2004)
[4] Ziegler J F, Biersack J P and Littmark U *The stopping and Range of Ions in Matter*, Vol. 1, New York, Pergamon (1985)

# Ion induced DNA damages

Lacombe S.*, Le Sech C.*, Huels M.**

*Lab. des Collisions Atomiques et Moléculaires LCAM (UMR 8625), Univ. Paris Sud 11, 91 405 ORSAY cedex – France
** Dept. of Nuclear Medicine and Radiobiology, Faculty of Medicine, University of Sherbrooke, Sherbrooke, Québec, CANADA

Energetic ions represent the most efficient and volume selective mode of therapy for deep-seated & non-operable tumours, they are also abundant in space environments. Therefore knowledge of fast ion effects on DNA is essential for radiation risk assessment, or therapy.
Moreover, at tracks end and along ionising particle tracks in cells, low energy ions are ubiquitous and they enhance clustered DNA lesions, mutations, or cell death. Therefore the understanding of DNA damages induced by low energy ions is also of fundamental interest in radiobiology.

In a first part, the ***effects of high energy ions (MeV/a.m.u.) on DNA in solution*** will be shortly presented**.** The experiments, performed in the Medical Centre of Proton therapy (Orsay), show in particular that the addition of radio-sensitizers such as platinum containing molecules (ex:PtTC) induces significant increase of the DNA strand breaks. This is attributed to inner-shell ionisation of platinum atoms by secondary electrons emitted along protons tracks, followed by Auger electron deexcitation. Additional experiments, performed with a free radical scavenger, indicate that the major part of DNA damages is mediated by free radicals attacks (indirect processes). Indeed secondary electrons emitted during the Auger deexcitation of the platinum induce efficient water radiolysis, which creates clusters of °OH free radicals close to the DNA that can efficiently break the DNA strands. These results suggest a possible application to protocols associating proton therapy (hadrontherapy) and chemotherapy with molecules containing high-Z atoms.

In a second part will be presented the preliminary results on the ***effect of low energy ions (eV/a.m.u.) on dry DNA*** in order to better understand the direct processes involved in the ion-DNA interaction. These experiments (performed in the CHU of Sherbrooke-Canada) show that very low energy ions may induce DNA single and double strand breaks. This suggests that secondary ions produced along the tracks and primary ions slowed down at tracks end must play a role in the destructive processes of the biological medium.

# Low and High Energy Radiation Femtochemistry of Biological Interest

Yann-A. Gauduel, Yannick Glinec, Victor Malka

Laboratoire d'Optique Appliquée, CNRS UMR 7639, Ecole Polytechnique – ENS Techniques Avancées, 91761 Palaiseau cedex (France)

Time dependent elementary radical mechanism are attracting growing experimental and theoretical interests for oxidoreduction reactions relevant to radiation damages in biomolecular environment. The fundamental importance of understanding primary effects of ionising radiation on water, "the lubricant of life", is emphasized in fields such as electron transfer reactions, radical chemistry of proteins, DNA repair and radiobiology. The main aspects of this talk concern the innovating domain of low-energy (photons) and high-energy (relativistic electrons) radiation femtochemistry.

Concerning low energy radiation femtochemistry (LERF), elementary radical reactions such as concerted electron-proton transfer processes, two-center-three-electron bond making can be investigated on the time scale of molecular motions by using ultrashort optical pulses, multiphoton excitation-ionization processes and high time-resolved spectroscopy [1,2].

For high energy radiation femtochemistry (HERF), the course of early ionising events taking place in the prethermal regime (less than 1 x $10^{-12}$ s) remained totally unknown. The magnitude of primary ionisation events remains uncertain, depending on indirect approaches such as the inverse Laplace transformation of a concentration dependence of the solvated electron yield using scavengers or stochastic modelling of nonhomogeneous radiolytic events with Monte Carlo methods.

The very recent advent of powerful laser techniques (table-top terawatt Ti:Sa laser amplifier systems) and laser plasma interactions providing femtosecond high-energy electrons beams, typically in the 2.5-15 MeV range, open new opportunities for the direct investigation of caged electron-radical pairs in nascent aqueous tracks and biological environment [3]. In this context, the first *Femtolysis* experiment (*Femto$_{second\ radio}$lysis*) opens exciting opportunities for the real-time observation of high-energy radiation chemistry. The primary yield of a reducing radical produced in clusters of excitation-ionisation events (spurs) has been determined at t ~3.5 $10^{-12}$ s. These results would provide unique information on the early distribution of energy deposition, positive hole motion ($H_2O^+$) and primary processes linked to nascent proton and OH radical. We attempt to address open questions on elementary events induced by the interaction of high-energy electrons with aqueous environments and raise future challenges for the development of prethermal radical chemistry. High-energy femtoradical chemistry would clearly enhance the understanding of radiation-induced damages in biological confined spaces (aqueous groove of DNA and protein pockets).

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# Low energy electron interactions with porphine derivates

S. Ptasińska, S. Denifl, S. Feil, M. Winkler, P. Scheier and T. D. Märk

Institut für Ionenphysik, Leopold-Franzens Universität Innsbruck and Center for Molecular Biosciences Innsbruck (CMBI), Technikerstr. 25, A-6020 Innsbruck, Austria

The aim of studies concerning the interaction between electrons and biomolecules in the gas phase is to elucidate the basic processes that lead finally to the damage of living cells upon exposure to ionizing radiation. Recent experiments demonstrated that electrons, most notably at very low energies, are of prime importance in inducing strand breaks in DNA [1]. In line with these findings we previously investigated therefore the interaction of highly monochromatized electrons with molecules such as DNA/RNA components (nucleobases, nucleosides, deoxyribose and water) [2,3]. In the present rather novel study we have selected another biologically significant molecule for living beings, i.e. porphine, which is the simplest of a group of chelating agents called porphyrins. Porphine forms bonds to a metal ion through nitrogen atoms. Each of the four nitrogen atoms in the center of the porphine molecule can form a bond to a metal ion. Depending on the central metal ion, porphine constitutes also a major component of hemoglobin, chlorophyll and vitamin B-12.

In the present study we have investigated experimentally the electron induced formation of both positively and negatively charged product ions of porphine derivates (e.g. 5,10,15,20-tetraphenyl-21H,23H-porphine iron (III) chloride = P) using a high resolution crossed molecular beam apparatus. The dominant negative ions formed via free electron attachment reactions are two complementary fragments $(P\text{-}Cl)^-$ and $Cl^-$, with an extremely sharp zero eV resonance and a broad resonance structure in the electron energy range from up to 6 eV. In contrast to most of the simple biomolecules, here formation of a parent negative ion is observed. Additionally, the positive ion formation shows an unusual ordering of ionization energies for parent and fragment ions. Using a three sector field mass spectrometer we prove the evidence of two states of the parent ion. Moreover, recently we have started to investigate delayed unimolecular decomposition of product ions formed via inelastic interactions of electrons with this porfine molecule.

It is a pleasure to thank Prof. Bernhard Kräutler for valuable advice and support.

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# Energy deposition model at molecular level in tissue equivalent materials

G. García

Instituto de Matemáticas y Física Fundamental, CSIC, Serrano 113-bis, 28006 Madrid, Spain.

In this talk we present a method to simulate the trajectories and single interactions, at molecular level, of electrons and photons in tissue equivalent materials. Methane based tissue equivalent materials are commonly used to fill some radiation detectors in medical and radiation protection applications. Since they absorb energy in a similar way to the soft human tissue, they give a direct measurement of the equivalent dose to be assigned in these applications. However, when microscopic detail is required it is necessary to check the behaviour of these materials in order to define the minimum size in which this approximation is valid. The foundation of our simulation program has been published in previous papers [1-2]. The main input parameters for this procedure have been the electron scattering cross sections both differential and integral that we have previously obtained for the constituent molecules (methane, nitrogen and carbon dioxide) as well as the energy loss spectra of electron in a mixture of these gases. The experimental system [3-4] and calculation procedure [5-6] to derive these data can be found in previous studies. We will finally give a microscopic energy deposition model that can be used to check the reliability of these materials in some biological application as a function of the energy of the primary radiation beam.

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# Conical intersections of potential-energy surfaces and ultrafast deactivation of excited electronic states

Wolfgang Domcke

Technical University of Munich, Department of Chemistry,D-85747 Garching, Germany

It is nowadays well established that conical intersections of electronic potential-energy surfaces are ubiquitous in polyatomic molecules and that they play a decisive role in photochemistry [1, 2, 3]. Ultrafast excited-state deactivation is an essential aspect for the photostability of the building blocks of life. The talk gives a nontechnical overview of generic aspects of time-dependent quantum wave-packet dynamics at conical intersections for representative ab initio based models. A simple qualitative picture is developed which allows us to rationalize how a conical intersection can effect an internal-conversion process within less than 50 femtoseconds. Evidence is presented that only few degrees of freedom are needed to descibe internal-conversion dynamics at femtosecond time scales, even in large systems. This opens the perspective of an ab initio treatment of elementary photochemical processes, provided that the few active degeees of freedom can be identified by ab initio calculations. The basic mechanisms which ensure the exceptional photostability of DNA bases and Watson-Crick base pairs are revealed by calculations on adenine and the guanine-cytosine base pair [4, 5, 6].

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# Which radiation track structure properties couple physical interactions to biological effects?

Herwig G. Paretzke

GSF-Institute of Radiation Protection, Ingolstaedter Landstr. 1, 85764 Neuherberg, Germany

Ionizing radiation is a primordial, ubiquitous stress to life, and biological effects to plants, animals, and humans of this physical agent after internal and/or internal exposure is of high scientific, political, and public interest.

It is mainly the low dose (< 100 mSv) and low dose rate (< 50 mSv per year) range were this interest is focussed (e.g. for exposures at the work place, in air travel, at home (Radon), in medicine (X-rays, PET and nuclear medical examinations), etc., etc.), whereas it is only for medium to high doses (say, 100 mSv to 4 Gray), where direct experimental evidence for such biological effects exist. Therefore, to satisfy the existent administrative needs of regulations regarding the limitations of exposures to low doses of ionizing radiation, from these valuable experimental data points extrapolations and interpolations have to be made over wide margins of parameter values and over many quantities. So, these extra- and interpolations have to be made regarding

a) the absorbed dose in biological matter (including the questions, whether "dose" is an appropriate quantity at all to characterize the amount of early physical disturbances of molecular targets i) in an irradiated cell, and ii) in a by-standing cell),

b) the rate at which this dose is inflicted upon the biological target(s) (including fractionation, re-oxigenetion and cellular re-population questions),

c) the quality of the incident primary radiation in consideration of the moderated and created secondary fields (e.g. most of the absorbed dose due to low energy neutrons results from created photons in extended bodies),

d) the time between the first observation of a biological effect and the previous exposure,

e) the individual sensitivity of the irradiated biological object (plant, animal, human) with consideration of the irradiated organ, the particular radiobiological end-point (e.g. reproduction, leaf fall, acute syndroms, late somatic effects) and the environmental living circumstances,

f) the genetic background of populations (e.g. transfer of risk factors across sexes and nations, between different species),

g) the different radiobiological end-points in the same object (is there are correletion between the yields of double strand breaks after repair induced in cells in-vitro and in-vivo in a tissue? Which role do intra-histion-interactions play? Which causal roles do mutations, transformations, chromosome aberrations, cellular inactivations, etc. play in radiation carcinogenesis in the affected organ? in other organs?),

h) etc., etc.

Since the primary tracks of charged particles left behind in an irradiation set the initial boundary conditions for all sub-sequent biological re-actions to this disturbances, it is interesting to analyse, which correlations can be observed between early (molecular modifications in charged particle tracks after picoseconds) and late (e.g. many years after this insult) radiation effects in biological objects (plants, animals, humans). This tutorial paper will outline the different physical aspects of early tracks of different radiation fields in biological tissues, their possible empirical correlations with various, relevant biological end-points, and the still existent large problems in the mechanistic interpretation of radiation actions on complex biological objects.

# DNA damage, repair and mutagenesis following radiation exposure

Evelyne Sage

CNRS UMR 2027, Institut Curie, Centre Universitaire, 91405 Orsay, France

Exposure to ionizing radiation (IR) induces leukemia and other cancers, and damage caused in DNA are presumed to constitute a primary event in the initiation of carcinogenesis. DNA lesions comprise single-strand breaks (SSB), double-strand breaks (DSB), and base damage. In addition, multiply damaged sites (MDS) which comprise several (≥2) DNA lesions, including oxidized bases and strand breaks, distributed on both strands within ≤20 bp, have been predicted and observed. However, the distribution of the classes of DNA lesions induced by ionizing radiation, their spatial arrangement and their complexity may vary depending on the type of radiation (low *vs* high LET) and the mechanism involved (direct *vs* indirect). To insure genome stability, DNA repair mechanisms have evolved to remove or tolerate cytotoxic or mutagenic DNA lesions in an error-free, or in some cases, in an error-prone manner. Base damage and SSB are mainly eliminated by base excision repair, while there are two main pathways for DSB repair, homologous recombination which is error-free, and non-homologous end-joining which is error-prone. In lower eukaryotes, like yeast, homologous recombination is the major pathway, while in mammals non-homologous end-joining predominates. The use of either pathway also depends on the phase of the cell cycle. Interestingly, it has been postulated that clustered damage (MDS) might hamper base excision repair process, or enhance DSB formed as repair intermediates, leading to lethal events. When unremoved from the genome, DNA lesions lead to mutations or to lethality. Base damage mainly generates base substitutions, whereas DSB may lead to loss of genetic material. Depending on the location of these mutations, in important genes or not, the consequences may vary. In the meantime, mammalian cells respond to radiation by initiating a vast array of events in the nucleus, as well as at cell membrane and in the cytoplasm. Cellular response to DNA damage involves increased expression or activation of many early responsive genes, such as tumour-suppresor p53. Sensor proteins recognize DNA damage before or after processing, signal their presence to transducers, typically protein kinases, that amplify the signal by phosphorylating downstream target proteins. Typically, an activation of cell cycle checkpoints within minutes occurs. Cell cycle arrest gives time to cell to repair their genome. If a cell is too heavily damaged, activated p53 will drive it to programmed cell death, i.e. apoptosis. Recent studies have shown that apoptosis can also be initiated by non-nuclear events. The presence of multiple signaling pathways ensures either cell suvival, cell cycle arrest and DNA repair, or a timely elimination of heavy damaged cell to prevent proliferation of mutated clones and protect from cancer.

# Radiation-induced bystander responses

Kevin M. Prise

Cell & Molecular Radiation Biology Group, Gray Cancer Institute, PO Box 100, Mount Vernon Hospital, Northwood, Middlesex, HA6 2JR, UK

Radiation action in biological systems has been studied for many years with a DNA-based model of effect. This has assumed that direct DNA damage from energy deposition is the underlying trigger for downstream biological consequences of exposure. Central to this has been the induction of DNA double-strand breaks, with much research showing that the ability of cell systems to remove or repair these lesions is important. In recent years several responses have been observed which don't fit the criteria of the DNA-based paradigm. These have been termed "non-targeted effects" as there is not a direct relationship between dose-delivery to the DNA and biological response. Archetypal of these is the bystander response. This is where cells which have not been directly exposed to radiation, respond due to the fact that their neighbours have been irradiated.

The bystander response involves cell-cell communication by two possible routes. One is where signals are released from irradiated cells into the cell culture medium, transmitting effects to non-exposed neighbours. The second involves direct communication between neighbouring attached cells via specialised communication pores, called gap-junctions. A range of experimental studies have provided evidence for bystander responses in a range of cell types and for a range of endpoints including, mutations, chromosome damage, cell killing, apoptosis and cell transformation. A common feature is that bystander responses are predominantly observed after low dose exposure, and tend to saturate at high doses, in contrast to the increasing level of effect with dose measured for conventional radiation response.

Much of these studies have utilised novel technology to map bystander responses. One approach is to use a microbeam which allows radiation to be targeted to individual cells within a population so that bystander responses can be carefully mapped. Microbeams can produce charged particles, electrons or X-rays and these can be targeted to regions of individual cells to test for mechanisms of response.

The observation of bystander responses has provoked much debate as to their importance. The fact they are observed at low dose has suggested that they may be important in carcinogenesis and radiation risk and may call into question the Linear Non-Threshold model currently used for extrapolating risk from high dose to low dose. Limited *in vivo* data available to determine whether this may be the case and further research is required.

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# Supramolecular and subcellular effects of ionizing radiation

Bojidar Galutzov

Dept. Biophysics and Radiobiology, Sofia University, Sofia, Bulgaria

DNA represents only 0.25% of mammalian cell content, and the percentage of DNA sequences coding proteins is no more than 1.5%. In the living cell DNA normally does not exist as free molecule, but forms supramolecular structures with a large number of proteins, which control the realization of the genetic information. The processes of replication, transcription and translation are realized by dynamic formations, with very complex relationships of their components. The radiation damage of some of them may be critical for the normal cell metabolism. The present state of our knowledge on the molecular mechanisms of cell regulation points the attention on other possible targets than DNA for the action of ionizing radiation. During the last three decades many new facts have been revealed by cell and molecular biologists concerning the fine cell structure and the complexity of cell functioning. In the light of these discoveries the radiation damage on living matter should be also considered not only at molecular, but also at supramolecular and subcellular level including cell organelles (endoplasmic reticulum, Golgi, lysosomes, peroxisomes). The role of mitochondria as a main energy supplier, their influence on cell apoptosis, the transport of ions and macromolecules and cell-cell signaling may Radiolysis of DNA binding proteins and functional consequences.

# Radiolysis of DNA binding proteins and functional consequences

M. Spotheim-Maurizot

Centre de Biophysique Moléculaire, CNRS, rue Charles Sadron, 45071 Orléans, France

Binding of a protein to its cognate DNA sequence is a key step in processes such as regulation of gene expression, DNA structuring or DNA repair. These fundamental processes may be disturbed if radiation destroys the DNA-protein complexes by damaging one or both partners. We have studied the effect of irradiation on three systems : i) the *E. coli* lactose operator-repressor complex [1, 2], ii) the complex between MC1, a DNA structuring protein of the archaebacterium *Methanosarcina,* and its cognate sequence in DNA [3] and iii) the complex between a DNA bearing an analogue of an abasic site and the repair protein Fpg of *Lactococcus Lactis* [4]. In all cases, we have observed that when irradiated in aerated solution, the complexes are disrupted mainly due to the damage to the protein. The irradiation of the free proteins induces the loss of their ability to bind DNA at even lower doses than those necessary to the disruption of the irradiated complexes. This difference of dose is due to the fact that in the complexes, the proteins are protected by the bound DNA.

All these effects are functional consequences of the modification of the amino-acids by the OH radicals produced by water radiolysis. The effect of the presence of an oxidation product on the structure and stability of the operator-repressor complex was estimated in a molecular modeling study [5]. The most probable sites of damage were identified *in silico* by using RADACK, a model that takes into account the accessibility and reactivity of each amino-acid [6].

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# Effect of estrogen receptor on radiation-induced damage to DNA

M. Běgusová[1] and V. Štísová[2]

[1]Nuclear Physics Institute, Academy of Sciences of the Czech Republic, Prague, Czech Republic
[2]Faculty of Nuclear Sciences and Physical Engineering, Czech Technical University, Prague, Czech Republic

Although radiotherapy and hormone therapy have been well established through a number of randomized studies, little is known about a possible interaction of both treatment modalities if they are given simultaneously. Radiotherapy and hormone therapy is combined in case of some types of breast cancer therapy. Estrogen signal is mediated within cells through specific binding to the estrogen receptor (ER). The estrogen – ER protein complex binds with an increased affinity to a specific DNA sequence, called hormone response element (HRE), and consequently the transcription is initiated.

Cellular radiosensitivity and radiation induced DNA damage (double strand breaks) in both hormone-sensitive and non-sensitive human breast cancer cell lines in presence or absence of estradiol were studied [Villalobos *et al.,* Int. J. Radiat. Biol. 70(2), 161-169, 1996]. The findings of this study indicate that (1) sensitivity to radiation and the proportion of proliferating cells are probably related, and (2) differences in radiosensitivity reflect differences in radiation-induced DNA damage.

The radiation damage to the specific complex between HRE DNA and ER protein at molecular level is the objective of the present study. The formation of the complex between irradiated DNA with nonirradiated protein and between irradiated protein with fresh DNA fragment have been determined and compared to the destruction of the complex by irradiation using retardation polyacrylamide gel electrophoresis. DNA fragmentation and distribution of strand breaks along DNA HRE base sequence have been determined on the denaturation sequencing polyacrylamide gel.

Theoretical modeling has been used to complement the study by predicting radiation attack of individual partners (DNA and protein) separately and bound in a complex. The relative yields of chemical reactions of $OH^{\cdot}$ radicals with reactive sites within specific DNA base sequence and binding domain of ER protein were calculated using the Monte Carlo method-based model RADACK (Běgusová *et al.* 2001, J. Biomol. Struct. Dyn. 19, 141).

The differences in the location of radiation damage in the free and bound DNA, the radiosensitivity of partners and its possible influence on the stability of the complex will be discussed.

# Biomolecular ions in accelerators and storage rings

Preben Hvelplund

Department of Physics and Astronomy, University of Aarhus, DK - 8000 Aarhus C, Denmark

With mass spectrometry we can now identify a substance in a sample by determining its molecular mass. Mass spectrometry is a very widely used method for small and medium sized molecules. By the use of electro spray ionization (ESI) and matrix-assisted laser desorption ionization (MALDI) macro-molecules can also be studied now a days. The trick is to get the macromolecules to fly or as the inven-tor of ESI John Fenn said in his Nobel lecture to give "wings to molecular elephants". Electrospray ionization has revolutionized the use of mass spectrometry to solve important problems in biology, bio-chemistry, biophysics and medicine. With electrospray ionization, it is possible to generate intact mul-tiply charged gas-phase ions from a variety of biomolecules. Mass spectrometry involving atomic ions started with the pioneering work by J. J. Thomson by the end of the nineteenth century and continued up through the twenties century. After a short historical introduction to mass spectrometry and a some-what elaborate description of electrospray ionization, examples of experimental investigations of bio-molecules in accelerators and storage rings will be presented [1]. These examples include measure-ments of geometrical cross sections of macromolecular ions, fragmentation of peptide and oligonucleo-tide ions after collisional electron transfer, lifetimes of excited ions, and radiative cooling. Statistical versus non-statistical decay after excitation in collisions or by photon absorption will be discussed. Topics included are also electron attachment to "naked" and microsolvated DNA and RNA nucleotide anions and the implications for structure changes in the Watson-Crick base pairs.

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# Ion induced fragmentation of DNA building blocks: isolated molecules and clusters

T. Schlathölter, F. Alvarado, R. Hoekstra, B. Manil*, J. Rangama*, B. Huber*

KVI Atomic Physics, Rijksuniversiteit Groningen, Zernikelaan 25, NL-9747 AA Groningen
*CIRIL-GANIL, rue Claude Bloch, BP 5133, F-14070 Caen Cedex 05

In the context of bio-molecular radiation damage, multiply charged ions (MCI) can be of importance as both, primary and secondary particles. Molecules within a cell can be subject to core ionization by a primary particle and subsequent Auger–cascades lead to formation of slow MCI. These ions in turn can interact e.g. with DNA constituents. As primary particles, for instance $C^{q+}$ ions are used in heavy ion therapy and also play a role in radiation exposure of biological tissue in space.

We investigate the interaction of keV MCI (typical kinetic energies within the Bragg-peak) with isolated nucleobases and nucleobase-clusters as model systems for DNA. MCI are extracted from an electron cyclotron resonance ion source biased at several keV and collided with the gas phase targets. Collision products are extracted by means of a static electric field and fragmentation is studied by coincidence time-of-flight spectrometry.

For 50 keV $C^{q+}$ we find a surprisingly weak dependence of the uracil fragmentation cross section and fragmentation pattern on the carbon charge state $q$. Because of its electronic structure unique amongst the $C^{q+}$ ions, only $C^{2+}$ leads to clearly different fragmentation dynamics. Only for this ion electron capture from the uracil HOMO can take place solely at very short ion–molecule separations, leading to extraordinarily strong fragmentation [1]. The spectra are essentially bimodal with a peak due to the parent ion and a broad distribution of small fragments [2]. Intact ions are formed in gentle overbarrier-like capture processes, whereas multifragmentation after close collisions leads to a broad distribution of small fragments. Triple coincidence studies reveal the origin of the most prominent peaks in the intermediate region: They are due to two-body breakup following a two-electron capture process. This fission process is accompanied by a most probable KER of 5.2 eV. Note that fagment ions with kinetic energies of a few eV only can to cause damage to nucleobases, as well [3].

For uracil, fragmentation always implies destruction of the ring, whereas for thymine also very weak channels associated with removal of atoms from outside the ring are observed. By embedding uracil into a cluster, we are able to study the effect of a surrounding medium on the ion-induced fragmentation. It is found, that fragmentation channels, which are forbidden in the isolated molecule, open up in the cluster case.

Furthermore, mixed $(\text{thymine}_n\text{adenine}_m)^+$ cluster-ions are found to follow non-statistical m/q distributions. These might be fingerprints of their geometric and electronic structure. Particularly the latter is exciting because of the possibility of Watson-Crick type hydrogen bonding known from DNA.

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# Sources, traps, and rings, which can be used for radiation damage experiments at the molecular level

H. Cederquist, M. Larsson, P.van der Muelen, S. Rosén and H. T. Schmidt

Physics Department, Stockholm University, AlbaNova University Center SE-106 91, Stockholm, Sweden

In this tutorial presentation, we will focus on a description of the principles of operation for a new facility for studies of interactions between positive and negative ions with low internal temperatures. This facility, DESIREE (Double Electrostatic Storage Ion Ring ExpEriment) is as the name suggests purely electrostatic allowing for storage of ions in a wide mass range from the lightest atomic ions to heavy bio-molecules. The unique features of DESIREE is that it may be cooled down to very low temperatures (about 4-5 K) by means of cryo-generators and the merging section for studies of interactions between ions of different charge states and masses at low and well controlled relative velocities (down to the sub eV region). In addition, the facility may be run in single ring mode for studies of interactions between positive or negative ions and laser light. The ultra low operating temperature of DESIREE has two advantages. First it strongly reduces the heat exchange between the stored ions and the vacuum vessel by a large factor and second it helps to reduce the residual gas pressure in the ring, which in turn makes long storage times possible.

In the build-up phase of DESIREE a large part of the effort will be devoted to means to prepare various types of ion beams (including bio-molecular beams) with low internal ion temperatures by means of electro-spray ion sources and temperature controlled pre-traps for ion bunching. At present there are two electrostatic storage rings in operation in the world [1,2] and apart from DESIREE [3] there is an additional one, CSR [4], under construction at the Max Planck Institute in Heidelberg.

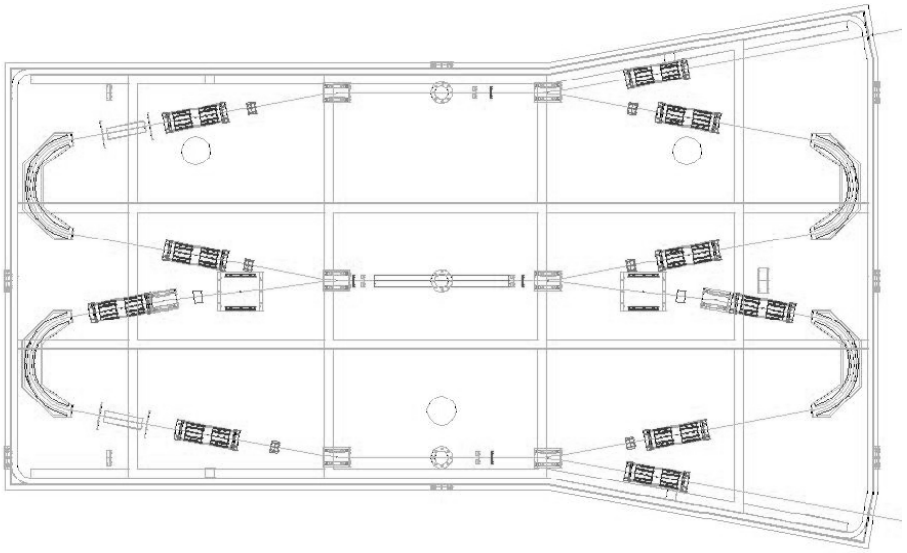

**Figure 1:** A schematic of DESIREE, which has two 9.2-m-circumference electrostatic storage rings with one common, beam merging section. The ring will be operated at 4-5 K and is equipped with an outer and an inner heat shield.

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# Ion-induced fragmentation and aggregation of small biomolecular systems

B. Huber

CIRIL/GANIL, Rue Claude Bloch, 14070 Caen, France

# Basic quantities in radiation physics including track structure

Bernd Grosswendt

Physikalisch-Technische Bundesanstalt, Bundesallee 100, 38116 Braunschweig, Germany

As is well known from radiation chemistry, the kinetics of radiation-induced systems strongly depends on the spatial distribution of atomic or molecular species produced by primary interactions of ionizing radiation in matter or, and this is the same, on the particle track structure. In view of this fact, far-reaching consequences on the development of living cells can also be expected if biological systems are exposed to ionizing radiation. In consequence, the knowledge of track structure and its description in terms of physical quantities, which are generally accepted and measurable (at least in principle) represent the basis of any multidisciplinary research concerning the physical, chemical and biological mechanisms involved in radiation-induced effects.

To put multidisciplinary discussions on the mechanisms of radiation effects on a sound basis, it is the aim of the present lecture to summarize a few of the most important physical quantities which are commonly used in the field of radiation dosimetry to describe the action of ionizing radiation in matter and of radiation quality, in particular. Central quantities to be used for this purpose are particle interaction quantities like *the mean free path length*, so-called radiation field quantities like *particle fluence*, the dose quantities *absorbed dose* and *kinetic energy released per unit mass* (kerma), and quantities like *particle range* and *linear energy transfer* (LET), which describe particular aspects of the energy transport by ionizing radiation. The greater part of these quantities is defined on a macroscopic scale. Nevertheless, to show their correlation to track structure, they will be described in terms of energy transfer points and of associated energy deposits of the tracks of single particles or of a multiplicity of particle tracks.

# Microdosimetric measurements of track structure quantities

S. Pszona

Soltan Institute for Nuclear Studies, 05-400 Otwock/Swierk, Poland

DNA molecules are still assumed as a main target of the biological effects of ionising radiation. More recently, clustered damage to DNA has been indicated as being of special importance. At this level the single particle interaction is responsible for the initiations of radiation damage to biologically important molecules. Therefore the track structure of an interacting particle at nonometre segments has to be taken into account.

The review of recently developed instrumentations for measuring nanosegment track structure quanities will be presented. Three different experimental approaches based on single counting mode will be shortly described with emphasizing the Jet Counting technique presently covering the largest range of nanometre size cavities. All appropaches are based on use of gas cavities for simulation of nanometric liquid water cavity.

The frequency distribution of ionization cluster size per single charged particle crossing a nanometre target is a new descriptor of radiation damage at DNA level.

The example of the frequency distributions of ionization cluster size for alpha particle and electrons will be given.

# Microscopic Target Structures in the Biophysical Simulation of Radiation Effects in Cells

Werner Friedland

GSF-Institute of Radiation Protection, Ingolstädter Landstr. 1, 85764 Neuherberg, Germany

In principle, the outcome of biophysical simulation calculations of radiation damage reflects characteristics of track structures of the ionising radiation on one hand and features of target structures on the other hand. It is essential to base the simulation in both areas on suitable microscopic descriptions of the real situation.

DNA damage response processes in cells are believed to be of critical importance to the post-irradiation development of cancer. Detailed information on DNA damage response and repair can contribute significantly to judgements on cancer risk at low doses. Of particular importance is the induction by radiation of complex forms of DNA double strand breaks and the problems experienced by cells in correctly repairing these complex forms of DNA damage. Therefore, biophysical simulation of these processes has to start with a simulation of the spatial and temporal structure of initial DNA damage, and this was an issue since the 80ies of the last century.

The first DNA target model represented the helix by a cylinder and divided its volume between bases and sugar-phosphate groups. It was rather successfully used in calculations of DSB yields and provided also quantitative information about the complexity of DSBs for different radiation qualities. However, this model was limited to DNA damage patterns within short genomic scales of 50 bp and did not consider DNA attachment to nuclear proteins in cell nuclei. These limitations were overcome by atomic models of the DNA, particularly after inclusion of higher-order DNA structures (nucleosomes, chromatin fibers, chromatin fiber loops, loop domains and chromosomes). Furthermore, the influence of the inhomogeneous target structure on DNA damage was taken into account by such models.

Calculated DNA fragment distributions using different models of chromatin fiber structures were found to be rather independent from radiation quality in the size range between 0.2 and 2 kbp but reflected proximity conditions of the fiber geometry. Comparison with measured fragment distributions elevated the simulations to a useful tool for biological microstructure analysis.

For larger DNA fragments in the size range from a few kbp up to some hundred kbp, an increased production, compared to random breakage, was observed in several experiments after high LET irradiation. Recently, PARTRAC calculations for N ion induced DSBs and DNA fragments were found in good agreement with corresponding experimental data. Another successful test for the DNA model in that size range was a simulation of $hprt^-$ deletion mutations which gave additionally indications for possible induction mechanisms.

Presently, two diverse approaches for the description of the genome are used in the biophysical simulation code PARTRAC. In addition to their presentation, trends in future model development will be pointed out.

**Acknowledgment**. Work supported by the European Union (contract no. FI6R-CT-2003-508842, "RISC-RAD").

# Modelling the evolution of radiobiological damage with focus on target structures

A. Ottolenghi, D. Alloni, F. Ballarini, D. Scannicchio

Dipartimento di Fisica Nucleare e Teorica Università di Pavia, and INFN, sezione di Pavia, via Bassi 6, I-27100 Pavia, Italy

Our knowledge of the stochastic, multi-step processes underlying radiation-induced biological damage can widely benefit by mechanistic models based on Monte Carlo simulations. Fundamental requisite in such codes is an appropriate description of the structure of both radiation tracks and target models, the latter to be reproduced with different levels of detail also depending on the specific endpoint of interest. Typical modelling scales at the sub-cellular level are nanometres for DNA and microns for chromosomes.

Concerning DNA damage, reviewed in the presentation by Werner Friedland (GSF), examples of studies carried out applying the PARTRAC code to different target structures will be presented. More specifically, the induction of SSB, DSB and more complex damage by various radiation types was simulated in naked DNA, SV40 minichromosomes and compact chromatin, thus allowing quantification of the protection provided by histones with respect to free-radical attack.

At the chromosome level, the main features of a Monte Carlo code providing dose-response curves for chromosome aberration induction will be illustrated. Examples of results compared with experimental data will be discussed, as well as applications to cancer risk estimation, in particular for Chronic Myeloid Leukaemia. The adopted target model is based on explicit description of interphase chromosome territories, each territory consisting of the union of small cubic boxes with volume proportional to the DNA content. Separate chromosome arm domains are under implementation. Examples of analogous models developed by other groups (e.g Cremer, Kreth *et al*.) will be discussed.

Finally an overview will be provided on non-targeted phenomena such as bystander effects, which indicate that the target of interest for radiation damage might be larger than the cell nucleus and even the cell itself. The main features and possible mechanisms characterising these effects will be outlined, including differences between the *in vitro* and *in vivo* conditions. Possible implications for low-dose risk assessment will be discussed, since bystander effects might imply that the Linear No-Threshold hypothesis does not necessary hold at doses of interest for radiation protection.

**Acknowledgment**. Work supported by the European Union (contract no. FI6R-CT-2003-508842, "RISC-RAD").

# Free-radical DNA Damage and its Repair – a Chemical Perspective

Clemens von Sonntag

Max Planck Institut Mühlheim (Ruhr), Bleichstr. 16, 45468 Mühlheim, Germany

A monograph with the above title will appear at Springer this year. Although it largely deals with chemical mechanisms, it is intended to easily understood also by scientists working in this area whose educational background is not chemistry. Radiation-induced damage will be dealt with in some detail, since our present knowledge of free-radical DNA damage is largely due to studies using ionizing radiation as a free-radical source. However, increasingly work is getting published where the damage is set specifically by a single radical. This allows us to come up with detailed mechanistic concepts. Clustered damage as induced by ionizing radiation but also by some anti-cancer drugs such as bleomycin and neocarzinostatin increases the severity of the damage. Some of these, the tandem lesions, are induced by a single radical. DNA damage can be modified at the free-radical stage. Hence the mechanisms of 'chemical repair', the 'oxygen effect' and radiosenitization are discussed in some depth. The chapters on DNA and directly related to DNA such as on nucleobases, nucleosides, nucleotides, polynucleotides and the detection of DNA damage are supplemented by general chapters that address more general aspects of free-radical chemistry: formation of free radicals in aqueous solution, reactions of OH radicals and H atoms, carbon- and heteroatom-centered radicals, polymer radicals and peroxyl radicals. More than 2.500 references will lead the reader to the pertinent literature.

Some selected items will be discussed.

# Abstracts

## Posters

# A coincidence study on ion-induced $H_2O$ dissociation

F. Alvarado, R. Hoekstra, T. Schlathölter

KVI Atomic Physics, Rijksuniversiteit Groningen, Zernikelaan 25, NL-9747 AA Groningen

Irradiation of malignant tumors with MeV ions has become a standard treatment in cancer therapy. Particularly the use of protons has proven to be very successful, e.g. at the Hahn-Meitner Institute for treatment of Choroidal melanomas of the eye. Over the last decade, the use of heavier ions for treatment of deeper-seated tumors has developed into a viable technique. Due to the high LET, ion irradiation is often superior to conventional radiation therapy using ultra-hard X-rays or MeV electrons. Within their ionization tracks, the ions deposit a large amount of their energy by ionization of water molecules, leading to formation of radicals, low energy electrons and (multiply charged) molecular fragments.
Very recently, absolute cross-sections for keV proton [1], $He^{q+}$ [2] and $Ne^{q+}$ [3] induced $H_2O$ ionization and fragmentation have been presented. Particularly for the more highly charged projectiles, Coulomb explosion of the transient multiply charged water ion was invoked to explain the obtained fragment kinetic energies. Due to non-coincident determination of the dissociation products, however, the assignment of kinetic energies to particular dissociation channels remained tentative.

We studied the (dissociative) ionization of isolated water molecules induced by impact of keV protons and $He^{q+}$ ions by means of coincidence time-of-flight (TOF) technique. Cations from ion induced water ionization and fragmentation were extracted into a reflectron-type TOF spectrometer by means of a weak static electric field. Coincident detection of two fragments from one dissociation event and high resolution of the respective fragment kinetic energies allows an unambiguous assignment of the respective dissociation channel to a kinetic energy release (KER). Surprisingly high intermediate charge states of the water molecule are observed.

For $He^+$ projectiles, we observe a strong $O^+$+$H^+$ fragment channel associated with a KER of about 15 eV. This value is much too low to be due to a Coulomb explosion of $H_2O^{3+}$. It is much higher, though, than the 5 eV KER observed for the (weak) $H_2O^{2+}\rightarrow OH^+$+$H^+\rightarrow O^+$+H+$H^+$ channel in photoionization studies[4]. Nobusada *et al.* [5] have theoretically predicted that if $H_2O^{2+}$ is formed by removal of the 2 most loosely bound $1b_1$ electrons (from the O lone-paired 2*p* orbital) accompanied by a shake-up of an electron from $3a_1$ to $4a_1$, then another sequential decay process occurs: $H_2O^{2+}\rightarrow OH^{2+}$+H$\rightarrow O^+$+$H^+$+H. The $OH^{2+}$ Coulomb explosion in the second step involves a KER of 15 eV in agreement with our observations.

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# Ion induced damage to DNA building blocks – a systematic study

Fresia Alvarado, Sadia Bari, Ronnie Hoekstra and Thomas Schlathölter

KVI Atomic Physics, Rijksuniversiteit Groningen, Zernikelaan 25, NL-9747 AA Groningen

The biological effects of ionizing radiation in living cells are not a mere result of the direct impact of high energy quanta of radiation. A primary particle interacting with individual molecules leads to molecular excitation, ionization and fragmentation. In the process, the primary particle looses energy and secondary particles such as low energy electrons, radicals and (multiply charged) ions are formed within the track. The interaction of these secondary particles with biologically relevant molecules is responsible for a large fraction of the induced biological damage in the cell.

In this context, multiply charged ions can be of importance as both, primary and secondary particles. Molecules within a cell can be subject to core ionization by a primary particle and subsequent Auger–cascades lead to formation of multiply charged ions. These ions in turn can interact e.g. with DNA constituents. As primary particles, for instance $C^{q+}$ ions are used in heavy ion therapy and also play a role in radiation exposure of biological tissue in space.

We investigate the response of isolated nucleobases, deoxyribose and nucleosides as model systems for DNA upon interaction with keV singly and multiply charged ions. The ions are extracted from an electron cyclotron resonance ion source biased at several keV and collided with the gas phase targets. Collision products are extracted by means of a static electric field and fragmentation is studied by coincidence high resolution time-of-flight mass spectrometry. We study the dependence of ionization and fragmentation of the targets on ion atomic number, charge state and velocity of the projectiles. Also we study the effect of the target molecule.

Previous studies on the isolated nucleobases uracil and thymine have shown that the fragmentation process can be divided into three regimes: i) non-dissociative ionization, ii) multi-fragmentation and iii) two-body break up [1]. These studies established a weak dependence of the fragmentation pattern and the fragmentation yield on the projectile itself but left open questions regarding the strong dependence of the fragmentation process on the properties of the target molecule. In other words how far is radiation damage to single nucleobases representative for damage to DNA?

To answer this question, we perform systematic studies on ion induced radiation damage of additional nucleobases, as well as sugars and nucleosides in order to understand their role as building blocks of macromolecules such as DNA and RNA.

Until now, for instance for gaseous deoxyribose only dissociative electron attachment studies have been performed [2]. Our experiments indicate that the keV ion induced fragmentation of deoxyribose exhibits the properties of statistical fragmentation, i.e. the fragment distribution follows a power-law. Almost no surviving molecules are observed. This is completely different from the nucleobase case and indicates that the sugar represents a much weaker structure within the DNA than the nucleobases do.

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# Absolute electron scattering cross sections of TriEthylamine in the energy range 20 ev-1.0 kev

W. Y. Baek and B. Grosswendt

Physikalisch-Technische Bundesanstalt, Bundesallee 100, 38116 Braunschweig, Germany

Within the framework of a project launched with the aim of the assessment of radiation damages to biological systems on a nanometric scale, double differential scattering cross sections were measured for electrons in TEA (triethylamine), which is used as a counting gas in the so-called OPAC (optical particle track chamber) detector1). It was developped at the Physikalisch-Technische Bundesanstalt in Germany and has been successful in resolving the spatial distributions of energy depositions by ionizing radiations on a length scale which corresponds to about 40 nm in tissues.

The measurements were carried out for primary electron energies from 20 eV to 1.0 keV, at scattering angles from 30° to 120° using a crossed-beam experiment. The measured energies of secondary electrons ranged from 4 eV to 250 eV. The cross sections were measured absolutely. This was made possible by the determination of the effective scattering volume, first by means of the attenuation of the primary beam current after crossing the molecular beam, and second by means of the total electron scattering cross section, which were measured before in a linear transmission experiment.

The results of these measurements were compared with the measuring results of other organic molecules. In addition, the applicability of scaling laws was investigated, using the cross sections of atoms or smaller molecular groups constituting TEA.

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# Reactions of Hydrated Electrons with Model Molecules for Bonds in Proteins

M.K. Beyer, Z. Sun, O. Petru Balaj, M. Gruber, and V. E. Bondybey

Technische Universität München, Department Chemie Lichtenbergstraße 4,
85747 Garching, Germany

Gas phase hydrated electrons are used as model reactors for elementary steps in the radiation damage of biological systems. $(H_2O)n^-$, n = 30 – 70, are generated by laser vaporization of a solid zinc target and supersonic expansion of the hot plasma in a helium/water mixture into high vacuum. The clusters are transferred to and stored in the cell of a Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometer. In the absence of collisions, hydrated electrons are stable for several seconds in the cluster, because the typical recombination partners from bulk aqueous solution, like $H^+$, $O_2$, and $CO_2$, are absent [1]. Volatile reactants are introduced at a steady background pressure, and the progress of the reaction is followed by recording mass spectra after varying reaction delays [2].

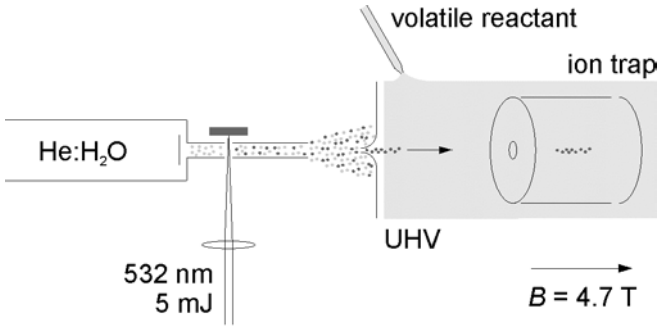


**Figure 1**: Hydrated electrons are generated with a laser vaporization source, and stored in the trap of an FT-ICR mass spectrometer, where they are reacted with volatile model molecules in binary collisions at a defined rate.

In the present study, N,N-dimethylformamide HCON(CH3)2 and dimethyldisulfide CH3S2CH3 were chosen as model molecules for the peptide bond and the disulfide cross-link in the cystine residue, respectively. $(H_2O)n^-$ take up N,N-dimethylformamide by ligand exchange, but the peptide bond is obviously unaffected by the nearby solvated electron. Dimethyldisulfide is also taken up by the clusters, but with a branching ratio of 10%, the disulfide bond is cleaved.

Compared with available results from pulsed radiolysis studies [3], as well as low energy electron attachment to neutral molecules in the gas phase [4], these new mass spectrometric studies of hydrated electrons in a finite cluster seem to provide complementary information to those widely established techniques. However, the technique is so far limited to very volatile, small model molecules.

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# Oxidation of methionine-containing peptides: spectral and conductometric pulse radiolysis studies

K. Bobrowski[1], D. Pogocki[1], G. L. Hug[2], B. Marciniak[3], C. Schöneich[4]

[1]Department of Radiation Chemistry and Technology, Institute of Nuclear Chemistry and Technology, 03-195 Warsaw, Poland
[2]Radiation Laboratory, University of Notre Dame, In. 46556, USA
[3]Faculty of Chemistry, Adam Mickiewicz University, 60-780 Poznan, Poland
[4]Department of Pharmaceutical Chemistry, University of Kansas, Ks. 66047, USA

In oxidative stress and biological aging, there is evidence that methionine radical cations are often implicated in the oxidative damage to peptides and proteins caused by reactive oxygen species (ROS). The progress of these reactions in real biological systems like proteins is difficult to unravel in vivo because of the complexity of the chemical environment. Therefore, by investigating model compounds: N-acetyl-methionine amide (N-Ac-Met-NH2), [1] a simple chemical model for the methionine (Met) incorporated in a peptide, and N-acetylmethionine methyl ester (N-Ac-Met-OMe), we were able to demonstrate sulfur-oxygen bond formation between Met(>S+•) and an amide/ester carbonyl group, respectively [2]. These observations confirm that the one-electron oxidation of organic sulfides is catalyzed by neighboring groups containing electron-rich heteroatoms, which stabilize the forming sulfide radical cations. Moreover, by monitoring the time-development of radicals and radical ions following pulse radiolysis coupled to time-resolved UV-Vis spectroscopy and conductivity detection we have suggested a novel reaction pathway leading to the formation of a new sulfur-nitrogen bonded species and involving nitrogen localized N-terminally to Met. Furthermore, we provide a novel pathway for the conversion of methionine radical cations into $\alpha$ C-radicals. Similar time-development of radicals and radical ions was observed in two N-acetylated peptides N-Ac-Gly-Met-Gly and N-Ac-Gly-(Gly)2-Met-Gly-Gly-Gly, [2] and the cyclic analogue of linear L-methionyl-L-methionine dipeptide. These observations provide further experimental proof for the formation of S-O bonded radical cations and the intramolecularly S-N bonded intermediates after one-electron oxidation of Met in small peptides. Importantly, the ratio of S-N bonded species vs intermolecularly S-S bonded species increases with increasing peptide size, suggesting that in longer oligopeptides containing methionine, will be the dominant form of stabilized sulfur-centered radicals.

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# Photocatalytic Inactivation of Pathogenic Bacterial biofilms on Medical Implant devices.

M.A. Boyle[1], P. Dunlop[2], W. Sigrac[1], T. Byrne[2], J. P. O'Gara[1], K.G. McGuigan[1]

[1]Royal College of Surgeons in Ireland,
[2]Northern Ireland BioEngineering Centre, UUJ2

The mechanisms by which biofilms are resistant to antimicrobials are poorly understood. Despite this, there is an understanding that new antimicrobial therapies are needed. Titanium dioxide photocatalysis shows promise as an effective antimicrobial. For a practical application of this technology to work, greater advances are needed in relation to our knowledge of biofilms and the effects of $TiO_2$ upon them. Available publications reflect upon the photocatalysis killing effect of planktonic or free living cells. The positive results of these experiments have lead to not only commercial products but also a greater vision of future uses. Photocatalysis has the potential to be used in removal of biofilm formation on the surfaces of medical devices. In order for this potential to be fulfilled more research is needed in the area of photocatalytic sterilization of biofilms themselves and not free living less resistant bacteria. This poster illustrates the inactivation of clinically relevant bacterial strain *Staphylococcus epidermidis* using photocatalysis. We also show a qualitative killing of bacterial biofilm using powdered $TiO_2$ and a novel way of assessing biofilm growth on glass slides. Photocatalytic sterilization has great potential as a new antimicrobial technology. It is feasible that this technology could be utilized in the removal of potentially harmful biofilm formations.

# Proton emission following multiple electron capture in slow ion-molecule collisions

F. Frémont,[1] D. Martina,[1] O. Kamalou,[1] P. Sobocinski,[1] I. R. McNab,[2] F. R. Bennett,[3] and J.-Y. Chesnel[1]

[1]CIRIL, Unité Mixte CEA-CNRS-EnsiCaen-Université, Bd Mal Juin, F-14050 Caen cedex 4, France
[2]Physics, School of Natural Sciences, University of N. upon T., Newcastle upon Tyne NE1 7RU,
[3]UKCSIRO Minerals, P.O. Box 90, Bentley, Western Australia, 6982, Australia

The study of collisions between slow highly charged ions and molecular species has received much attention during the past few years. The studies have given detailed experimental and theoretical information on both the electron capture occurring during the collision and the fragmentation dynamics that takes place after the removal of the electrons from the target. However, for the case of multi-electronic molecular targets, many questions remain open because the electronic structure of a molecule differs strongly from that of an atom and both the electron capture and the subsequent fragmentation depend upon the chemical bonding within each electronic state of the molecule that contributes to the observations.

In the present work we studied the fragmentation of $HC\ell$ molecules following multiple electron capture by 98-keV $N^{7+}$ ion impact. The use of $HC\ell$ was motivated by the fact that in the $HC\ell$ fragmentation process conservation of momentum leads to $H^+$ fragments (of mass 1 a.u.) having a kinetic energy which is typically 35 times larger than that of the corresponding $C\ell^{q+}$ fragment (of mass 35 a.u.). This situation is similar to that of water molecules, whose fragmentation leads to Hfragments with high kinetic energies (compared to those of $O^{q+}$ fragments) [1]. Therefore, the dissociation of $HC\ell$ leads to fragments whose energies may easily be separated, even if a non-coincidence technique is used. The present experiments were conducted at the 14-GHz ECR ion source at GANIL in Caen. The fragments produced after the collision were detected at angles in the range from 20° to 160° with respect to the incident beam direction, and were energetically analyzed by using a single-stage spectrometer which consists of an electrostatic parallel-plate analyzer.

Proton fragments with energy as high as 100 eV were observed [2]. We have shown using the Landau-Zener model that the projectile mainly captures outer-shell electrons. Consequently, the Auger deexcitation of the target is expected to be negligible. Thus, our spectra indicate that the proton energy is directly connected to the number of captured electrons. Comparison with the simple Coulomb explosion model suggests that up to seven target electrons may be involved during the collision. Furthermore, from the fragment kinetic energy spectra, relative cross sections for multiple electron capture are deduced. The obtained cross sections are compared with results derived from both the classical over barrier model and the semi-empirical scaling law of Selberg et al. [2]. While large discrepancies are observed for the over barrier model, a reasonable agreement is seen when comparing with the scaling law.

This preliminary study shows that the present technique for measuring fragment energy distributions is an efficient tool to obtain information on the primary process (i.e. multiple capture). Since the data collection by using our technique is faster than that by means of more sophisticated methods, the present results open the way for investigating electron capture in $N^{7+}$ + $HC\ell$ collisions in a wide range of projectile energies (down to a few eV) and, thus, for providing data that are complementary to those recently obtained with $H_2O$ molecules [1].

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# Simulation of Ion Induced Radiation Damage

W. Friedland, P. Jacob and H. G. Paretzke

GSF-Institute of Radiation Protection, Ingolstädter Landstr. 1, 85764 Neuherberg, Germany.

Simulations of charged particle track structures in biological material represent an important tool for the analysis of radiation effects. The biophysical simulation code PARTRAC has been used in several studies of photon, electron, proton and recently [1] helium ion induced radiation effects like SSB and DSB induction, DNA fragmentation and $HPRT^-$ mutation induction. The calculated yields for such endpoints were usually found in reasonable agreement with corresponding experimental data, particularly after taking into account the boundary conditions in the determination of the experimental data.

Present activities in the development of the PARTRAC model are focused on a mechanistic simulation of the processes occurring within the biological stage subsequent to the initial radiation damage to DNA (and maybe other relevant targets) during the physical and chemical stage. Fundamental processes in the biological stage are the mechanisms of repair of genomic damage and processing of the residual damage in connection with intra- and intercellular signalling. The dynamics of these actions can be well studied by irradiation of cells with single ions from microbeam facilities in association with current visualisation methods [2]. Such experiments provide data which are indispensable for the development of a mechanistic description of the processes during the biological stage. In order to make use of them, the model has to allow a simulation of the initial damage under corresponding irradiation conditions.

To this end, the track structure part of PARTRAC has been extended by a new ion track module to cope with further ion particles besides hydrogen and helium. Cross section for ion-electron interactions are taken from doubly-charged helium ions of the same velocity and scaled by $Z^2/4$. This scaling law can be taken as a reasonable approximation for light ions of more than about 5 MeV per nucleon. For transport distances of less than 0.3 nm between succeeding interactions the location of the second one is allowed to deviate randomly from the beam line.

In order to test the ion track module in PARTRAC, calculations of the radial dose distribution were performed for tracks of $^{16}O$ ions with 21.2 MeV/nucleon. The results were found in excellent agreement with experimental data [3] and cited model calculations.

DNA damage due to irradiation of human fibroblast cells by ions of boron, nitrogen and neon was calculated for energies corresponding to experimental investigations [4]. The measured DSB yield per track was highly reproduced by the calculation after subtraction of the experimentally unresolved fraction of breaks, and the distributions of DNA fragments were found in accord as well. The calculations were complemented by corresponding data for He ions of various energy which exhibit in some respect rather different damage patterns. Furthermore, calculations have been performed for C-, N-, and O-ions of 6.25 MeV per nucleon initial energy in view of corresponding experiments underway [2]. The analysis of the radial distribution of energy depositions and DSBs is still in progress, results are going to be presented at the meeting.

**Acknowledgment**. Work supported by the European Union (contract no. FI6R-CT-2003-508842, "RISC-RAD").

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# Formation of ionization clusters in nanometric targets by electrons

Bernd Grosswendt

Physikalisch-Technische Bundesanstalt, Bundesallee 100, 38116 Braunschweig, Germany

The ultimate aim of any research in radiation physics is the understanding of specified physical, chemical or biological changes initiated in matter when exposing it to ionizing radiation. Here, the structure of particle tracks is of particular importance since the spatial distribution of interaction points and the accompanying excited species of target molecules are responsible for the type of chemical reactions or the succession of various chemical processes of a reaction chain initiated by primary radiation. In this context, the track structure of electrons is of great interest since they are set in motion in large numbers as secondary particles during the slow down of any kind of ionizing radiation in matter. From the point of view of radiation induced early damage to genes and cells, which starts with the early damage to segments of the DNA molecule, the most effective secondary electrons are those at energies of a few hundred eV since the yield of double-strand breaks induced by such electrons in the DNA shows a maximum [1]. This can be explained by the fact that in water cylinders, 2 nm in diameter and height (as a substitute to small segments of the DNA), the probability of the electron-induced formation of ionization cluster sizes greater than or equal to two is highest also at initial electron energies of a few hundred eV [2].

In view of this promising feature of ionization cluster-size distributions formed by low-energy electrons in nanometric targets of liquid water for explaining particular radio-biological endpoints, it is the aim of the present work to investigate the properties of cluster-size formation by electrons as a function of target size. Here, main emphasis is laid on the behaviour of cluster-size distributions if the target size is reduced from macroscopic to nanometric volumes.

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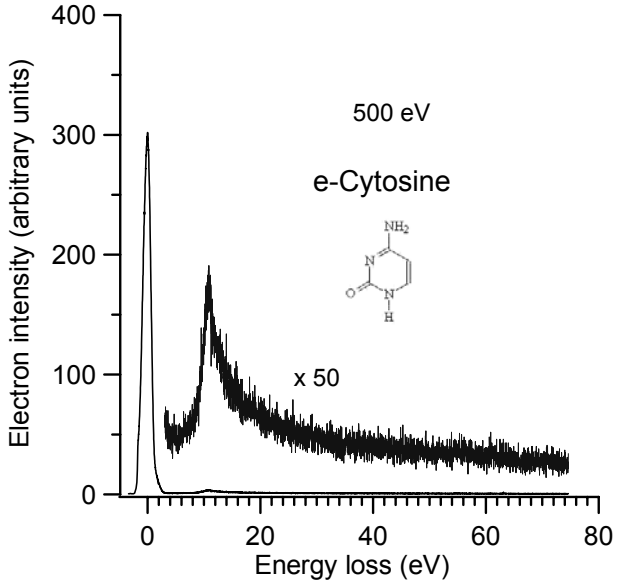
# Electron scattering from cytosine at intermediate and high energies

P. Kendall[1], J.C.Oller[2], F. Blanco[3], J. Rosado[4], P. Limão-Vieira[5], N. J. Mason [1] and G. García[4]

[1] Centre of Molecular and Optical Sciences, Department of Physics and Astronomy, the Open University, Milton Keynes, MK 6AA, UK
[2] Departamento de Electrónica y Automática, CIEMAT, Avenida Complutense 22, 28040 Madrid, Spain
[3] Departamento de Física Atómica, Molecular y Nuclear, Universidad Complutense de Madrid, 28040 Madrdi, Spain
[4] Instituto de Matemáticas y Física Fundamental, CSIC, Serrano 113-bis, 28006 Madrid, Spain.
[5]Dep. de Física & Laboratório de Colisões Atómicas e Moleculares, CEFITEC, Universidade Nova de Lisboa, Quinta da Torre, 2829 - 516 Caparica, Portugal

The experimental system used to the study of the electron interactions with molecules of atmospheric interest [1-2] has been adapted to work with DNA basis in the gas phase. For this purpose, an indirect heated oven by electron bombardment has been designed and constructed. First energy loss experiments for intermediate and high energy (100-5000 eV) will be presented. As an example, next figure shows the energy spectrum of 500 eV electrons crossing a molecular beam of cytosine.




In addition, a model potential calculation procedure based on a single atom representation, with screening corrections [3-4], has been applied to obtain the differential and integral elastic as well as the integral inelastic cross sections for electron scattering from cytosine in the energy range 10-10000 eV.

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# Energy deposition model at molecular level for ionisation chambers

A. Muñoz[1], J. M. Pérez[1], J. C. Oller[1], F. Blanco[2] and G. García[3]

[1]Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (CIEMAT), Avenida Complutense 22, 28040 Madrid, Spain
[2]Departamento de Física Atómica, Molecular y Nuclear, Universidad Complutense de Madrid, 28040 Madrid, Spain
[3]Instituto de Matemáticas y Física Fundamental, CSIC, Serrano 113-bis, 28006 Madrid, Spain

Ionization chambers are one of the most popular radiation detectors for photons. They provide a direct measurement of the radiation exposure rate. By assuming a charge equilibrium down the sensitive area of the chamber and introducing an average energy to produce each electron ion pair, this measurement is customary translated to an absorbed dose value. The validity of these approximations is strongly dependent on the production and dynamic of the secondary electrons. In this work we present an energy deposition model which includes the secondary electron interactions with the constituent molecules of the filling gas (commonly air). The model is based on a Monte Carlo simulation of the trajectories and interactions of primary and secondary particles along an extractive electric field. The basis of the method have been previously described [1-2] and it uses as input parameters the electron scattering cross sections we have previously measured [3-4] or calculated [5-6]. The energy deposition pattern of the secondary electrons is given by a normalised probability distribution function derived from the experimental energy loss spectra. The reliability of the absorbed dose assignment procedure in ionisation chambers will be discussed as a function of the energy of the primary particles.

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# Inelastic scattering and stopping power of electrons in tissue equivalent materials

A. Williart [1], J. Rosado[2], J. C. Oller[3], J. M. Pérez[3], A. Muñoz[3], F. Blanco[4] and G. García[2]

[1] Departamento de Física de los Materiales, UNED, Senda del Rey 9, 28040 Madrid, Spain
[2] Instituto de Matemáticas y Física Fundamental, CSIC, Serrano 113-bis, 28006 Madrid, Spain
[3] Departamento de Electrónica y Automática, CIEMAT, Avenida Complutense 22, 28040 Madrid, Spain
[4] Departamento de Física Atómica, Molecular y Nuclear, Universidad Complutense de Madrid, 28040 Madrd, Spain

Methane based tissue equivalent materials are commonly used to fill some radiation detectors in medical and radiation protection applications. Since they absorb energy in a similar way to the soft human tissue, they give a direct measurement of the equivalent dose to be assigned in these applications. Following the procedure we proposed in a previous study [1], we present the stopping power of electrons in a tissue equivalent material obtained as a mixture of methane, nitrogen and carbon dioxide. Electron energy loss spectra for this target have been obtained for incident energies ranging from 100 to 5000 eV by using the experimental system described in previous papers [2-3].
Integral inelastic electron scattering cross section values have been derived from those of the constituent molecules. The calculation procedure has been detailed elsewhere [4-5] and is based on a single atom representation with screening corrections.
Stopping power of electron have been finally determined by combining the cross section data with the mean energy loss derived from the experiment. The present results will be compared with those given by the Born-Bethe approximation [6].

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# Degradation of Gas Phase Biomolecules by Low Energy Electrons (< 3 eV)

S. Gohlke, H. Abdoul-Carime and E. Illenberger

Freie Universit ¨at Berlin, Institut für Chemie Physikalische und Theoretische Chemie, Takustraße 3, D14195 Berlin

The important role of secondary electrons in the primary molecular steps towards radiation damage has now widely been recognized [1]. Energy deposition by high energy quanta creates electrons as most abundant secondary species with initial energy distributions extending up to a few tens of eVs. These *ballistic* electrons are present in the medium within a short time window (fs – ps) thereby interacting with DNA and its environment. In the course of inelastic collisions, they can initiate further ionization and excitation processes creating reactive species like neutral radicals, ions and electrons. At sufficiently low energies they may either be captured at particular molecular sites or they will ultimately be trapped as solvated electrons. The interaction of *ballistic* electrons with the cellular material is hence essential to unravel the *initial* molecular steps in radiation damage. Very recent experiments showed the potential of electrons at even *subexcitation* energy (0 –4 eV) to effectively induce single strand breaks (SSBs) in plasmid DNA [2].

We present experiments on the gas phase nucleobases (NBs) thymine, cytosine, adenine and guanine demonstrating that any of the four bases exhibits a pronounced low energy resonance located near 1 eV (where SSBs were observed) leading to dehydrogenation according to the dissociative electron attachment (DEA) process [3]:

$$e^- + NB \rightarrow NB^{-\#} \rightarrow (NB–H)^- + H$$

$NB^{-\#}$ is the transitory negative ion (TNI) formed by resonant electron capture and $(NB–H)^-$ the closed shell anion formed by ejection of a neutral hydrogen radical. The reaction is operative already at subexcitation energies and energetically driven by the appreciable electron affinity of the (NB–H) radicals which is in the range between 3 and 4 eV [4]. Further experiments with partly deuterated thymine demonstrated that hydrogen abstraction is exclusively operative from the N sites [3]. These specific sites are involved in the binding of the nucleobase to the sugar backbone via the N1C glycosidic bond and to the complementary base through hydrogen bridges (via N3H), respectively. We finally show that gas phase thymidine (thymine bound to a sugar unit) effectively decomposes into the sugar and thymidine moiety with the negative charge localized on either of the units [5].

*Work supported by European Union through the Training and Mobility Network EPIC (Electron and Positron Induced Chemistry) and the Deutsche Forschungsgemeinschaft.*

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# Energetics of C2'-H hydrogen atom transfer between 2-deoxyribose and neutral radicals of hydrogenated pyrimidine bases

M. Gołębiowska[a], A. Sadowska,[a] P. Storoniak,[a] M. Śmiałek,[b] N. Mason,[b] M. Gutowski,[a,c] J. Rak[a]

[a]Department of Chemistry, University of Gdańsk, Sobieskiego 18, 80-952 Gdańsk, Poland
[b]Center of Atomic and Molecular Engineering,The Open University, Walton Hall, Milton Keynes, MK7 6AA, United Kingdom
[c]Chemical Sciences Division, Pacific Northwest National Laboratory, Richland, WA 99352, USA

Secondary electrons, one of the main species formed in water irradiated by high-energy particles, were proved to be responsible for single- and double-strand breaks in DNA [1]. The resonance pattern of the damage quantum-yield versus incident electron energy, observed by Sanche et al. [1], suggests that DNA damage proceeds via resonance anionic states probably localized in the nucleic base molecules. However, the rates of sugar-phosphate bond cleavage calculated for both the model resonance anions of nucleotides [2] and those of sugar-phosphate-sugar system [3] are too high to be competitive with electron autodetachement occurring at at ca. 1014 s-1 [4]. We, therefore, believe that the main channels leading to DNA strand breaks by low-energy electrons involve stable anionic states and the role of resonance states is only to allow for energy transfer between the impinging electron and the neutral target [4].

In this communication we focus on a mechanism where a reactive form of the nucleic base (radical) abstracts a hydrogen atom, C2'-H, from the 2-deoxyribose ring to bring about direct DNA strand scission. (is it clear that it will lead to a scission?) This type of mechanism explains, for example, the dissociation of a synthetic DNA fragment in which the natural thymine has been replaced by 5-bromouracil [5]. In our mechanistic proposal the reactive nucleic base radical is formed directly before the C2'-H abstraction as a result of barrier-free (or small barrier) proton transfer (BFPT) between a stable nucleobase anion and a proton donor (the BFPT process has been observed by us in numerous anionic complexes between nucleobases and proton donors [6]).

The energetics of C2'-H hydrogen atom transfer has been calculated for all possible neutral hydrogenated radicals of pyrimidine bases. We have found that the process involving radicals formed due to proton transfer to the C6 position of uracile and cyitosine anions and the C5 position of anionic thymine is accompanied with the smallest theromodynamic barrier. This barrier amounts to 6.5, 9.0, and 9.4 kcal/mol at the B3LYP/6-31++G** level and to 4.6, 8.7, and 13.8 kcal/mol at the PM3 level for uracil, cytosine and thymine radicals, rescpectively. Although these values are somewhat too big to assure high yield of the damage, one should remember that DNA geometrical constraints as well as influence of environment have not been accounted for in our computational model.

**Acknowledgments***:* This work was supported by British Polish Research Partnership Programme (J.R. and N.M.; grant no. WAR/341/257) and the US DOE, Office of Biological and Environmental Research, Office of Science, Low Dose Radiation Research Program (M.G.).

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# Ab initio study of metalated non-complementary DNA base pairs

Leticia González and Marko Schreiber

Institut für Chemie und Biochemie, Freie Universität Berlin,
Takustrasse 3, D-14195 Berlin, GERMANY

It is known that some metals ions stabilize tautomers of DNA bases disturbing DNA replication processes. Depending on the metal-binding site, the complexation can result in stabilization or desestabilization of the nucleobase, supporting or preventing pairing of nucleic acid bases, respectively. The silver cation, $Ag^+$, is argued to be one of the most important nucleic base binding metal ions. It has a preference for binding to endocyclic nitrogen atoms and thus catalyses the formation of non-Watson-Crick base pairs.[1]

Our goal is used laser radiation to eliminate metal ions in non-Watson-Crick base pairs. Because there is little information on non-complementary base pairs, our very first step is to determine the structure of metalated base pairs complexes. In this poster we present Ag(I) complexes of adenine-cytosine DNA base pairs. Because metal ions can also stabilize rare forms of nucleobases, we have first determined the binding position of $Ag^+$ in adenine and cytosine DNA bases. The calculations are done using the ab initio MP2 method with the cc-pVTZ basis set for the main group atoms and the MWB effective core potential for Ag.[2] Our results indicate that the most stable Ag-adenine complex does not correspond to the canonical form, while this is the case for Ag-cytosine. Where possible, N—Ag—N or N—Ag—O bridges are favored. This geometry is, however, not characteristic of metalated base pairs, where almost linear N—Ag—N or N—Ag—O arrangements are observed. Preliminary results for the electronic excited states of stable metalated base pairs will be also presented.

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# Combined electron emission effects on the biologically damaging efficiency of 125I

A. Grau Carles

IMAFF/CSIC, Dcho. 211, C/ Serrano 113b, 28006 Madrid, Spain

Understanding the strong radiotoxicity of DNA-incorporated Auger electron-emitting nuclides requires a detailed knowledge of the physical processes involved in the rearrangement of the electrons within the atom, after an inner shell vacancy is created by the decay process. The decay of 125I entails the copious emission of low-energy electrons, resulting, in many cases, in a highly charged daughter atom. This generates a large density of electron irradiation in the vicinity of the decay site, and explains the observed fact that the biological action of Auger emitters depends significantly on the location of the radionuclide into the cell. When 125I is incorporated outside the cell nucleus, relatively non-toxic effects are observed [1]; on the contrary, the intranuclear incorporation of 125I generates important cellular damages, such as DNA strand breaks [2], mutations [3] and chromosome aberrations [4].

One important obstacle in the microdosimetrical analysis of the biological damage of 125I arises from the collective effects of the emitted electrons. Some atomic rearrangement pathways have a non-negligible probability of emitting only electromagnetic radiation, which can easily escape from the cell nucleus without interaction. On the other hand, the simultaneous emission of several electrons with energies greater than 0.1 keV is also possible form the decay of a single atom of 125I. In such a way, the biological action can be radically different depending on the considered atomic rearrangement pathway.

Over the past two decades, a simplified KL1L2L3M model of only 256 atomic rearrangement detection pathways has been developed for the determination of the specific activity of 125I samples in liquid phase [5]. The procedure, today called the CIEMAT/NIST method [6], requires to carry out the measurements in a liquid scintillation spectrometer. Since the response of the detector is nonlinear to low-energy electrons, the relative contribution of the emitted electrons for each pathway must be computed. In this work we tabulate separately for each atomic rearrangement pathway: its probability, the energies of the emitted electrons and the absorbed dose in different size liquid water microspheres.

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# Photochemical studies of oligodeoxyonucleotides duplexes containing 5-bromouridine and 5-bromocytidine

M. Jasionowski[a], M. Śmiałek[b], N. Mason[b] and J. Rak[a]

[a]University of Gdańsk, Department of Chemistry, Sobieskiego 18, 80-952 Gdańsk
[b]Center of Atomic and Molecular Engineering, The Open University, Walton Hall, Milton Keynes MK7 6AA, United Kingdom

Replacement of thymidine by isosteric 5-bromouridine in DNA makes this biopolymer sensitive to damage induced by UV or γ-radiation. Irradiation of DNA duplexes containing such modification produces single and double-strand breaks as well as alkaline labile lesions in nucleotides adjacent to BrdU. However, the mechanism of strand break formation induced by UV light is not yet clear [1,2]. The probable reaction sequence might involve photoinduced single-electron transfer to 5-bromouridine [3] followed by BrdU dehalogenation resulting in deoxyuridin-5-yl, which, in turn, abstracts hydrogen from the C1' or C2' of the adjacent deoxyribose. The deoxyribose radical formed in the last step stabilizes via hydrogen shifts, and a strand break finally occurs.

In the present studies we investigated the efficiency of UV-damage to the model short DNA fragments containing BrdU and BrdC. Products of UV-induced cleavage of DNA duplexes were analyzed using PAGE electrophoresis, RP-HPLC method and MALDI-TOF spectrometry. The composition of the photolyte indicates formation of water attachment products and hydrolysis of the N-glycosidic bond between the nucleic base and the deoxyribose residue.

**Acknowledgments**: This work was supported by British Polish Research Partnership Programme (grant no. WAR/341/257)

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# Contribution to the Physical Stage of the Water Radiolysis using Imaging Techniques

S. Legendre, M. Tarisien, L. Adoui, A. Cassimi, B. Gervais, E. Giglio

CIRIL/CEA/CNRS/ISMRA, Rue Claude Bloch, BP 5133, F-14070 Caen Cedex 5, France

Water radiolysis represents an important field of research in a great number of fundamental or applied physical processes. For example, from the radiobiological point of view, the greatest part of the energy deposited by ionizing radiations in biological matter is absorbed by water molecules, leading to formation of various radicals or molecular species. The majority of the experimental as well theoretical studies undertaken in the case of high Linear Energy Transfer (LET) ions were dedicated to the chemical stage of radiolysis. The lack of information relative to dissociation of ionized water molecules makes very complicated simulations of the physico-chemical stage of the problem. We propose (using imaging techniques based on multicoincident detection of the fragments) to perform experiments dedicated to the study of water molecule fragmentation induced by collision with multiply-charged ions. Beyond dynamics information such as KER distribution measurements or selectivity of the bond breakage, that we will have in a simultaneous way, the prime objective will be to study the importance of ***multiple ionization*** for different LET values as well as the identification of ***dissociation pathways*** and ***branching ratios*** for each ionization level of the molecule $(H_2O)^{q+}$.

Of course, the question arises to know whether one can extrapolate the results obtained in gas phase to liquid water radiolysis. We propose, in a second time, to study the influence of the medium density by studying ionization of water clusters. Even small, these clusters have distances between closer neighbors near to those observed in condensed phase. The possibility will thus be given of studying the influence of neutralization of the primary species produced.

# Collisions between protons and biomolecules: electron emission and molecular fragmentation

A. LePadellec, P. Moretto-Capelle

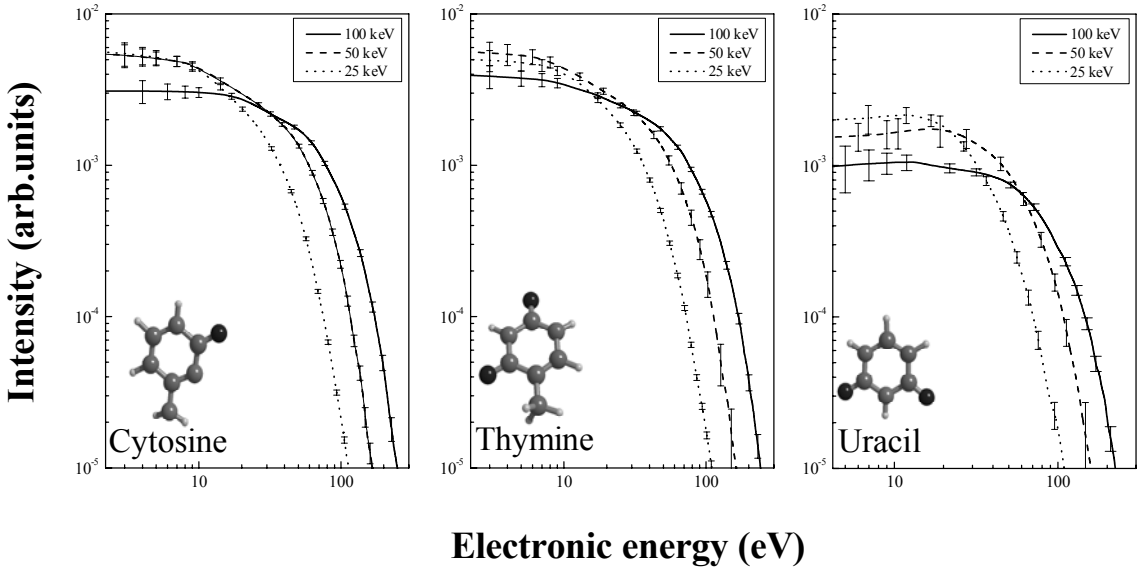
IRSAMC, LCAR, UMR-5589 CNRS-Univ.P.Sabatier
118, rte de Narbonne, 31062 TOULOUSE CEDEX, FRANCE

Damages induced by ionizing radiation can directly be linked to alteration of the DNA molecule. In this work, we have investigated interactions between protons and phase gas pyrimidic bases (uracil, cytosine and thymine) in the 25-100 keV energy range,the latest collision energy corresponding to the formation of the Bragg peak in biological medium. We have considered:

i) direct effects on bases such as ionization and fragmentation studied by coincidence time of flight techniques [1]

ii) secondary electron emission. During the interaction, electrons are also emitted which can also interact with the neighboring molecules and be responsible for other damages depending on their kinetic energy [2,3] . The electron spectra (see figure 1) show the importance of low energy electrons.

Figure 1: Electron spectra measured in H++ bases collisions observed at 35° with respect to the beam

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# *Ab initio* study of intermolecular interactions in neutral and ionized biomolecules

E. Cauët[a], C. Biot[b], R. Wintjens[c], M. Rooman[b] and J. Liévin[a]

[a] Service de Chimie Quantique et Photophysique, [b] Unité de bioinformatique génomique et structurale, [c] Chimie générale, Institut de Pharmacie
Université Libre de Bruxelles, 50 Avenue F. D. Roosevelt, B-1050 Brussels, Belgium

Intermolecular interactions contribute significantly to the stability and conformation of biomolecules such as DNA, proteins and their complexes, but the role they play in reactive processes related to radiation damage in such biomolecules is still not well known. It would thus interesting to investigate this problem by means of quantum chemical calculations. This is unfortunately not an easy task for such large systems because intermolecular interactions require the use of the highest levels of quantum methods in order to take exchange and dispersion correlation effects properly into account. Moreover the solvent effect should ideally also be considered. In this work, we present a systematic *ab initio* study of intermolecular interactions in neutral and ionic model biomolecular systems.

Three kind of interactions occuring simultaneously in biomolecular complexes have been investigated: π-stacking, H-bonding and cation-π interactions. The model systems used to mimic the interface of such complexes are: stacked DNA base pairs, complexes of histidine with phenylalanine and adenine and complexes of stacked DNA bases with a positively charged protein residue. Systematic methodological tests are presented, leading to the definition of the basis set and the method of calculation to be used. We show that using the MP2 method and the medium size 6-31G** basis set augmented by an optimized diffuse d polarisation orbital allows a correct estimate of the complexes binding energies [1]. The solvation effect is investigated by using the IEF-PCM model in the case of the histidine-aromatic complexes.

The study of the ionization of the DNA bases (monomers and dimers) are presented in another poster. The methodological tests are presented here.

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# VUV electronic state spectroscopy of water

R Mota [1], R Parafita [1], N J Mason [2] and P Limão-Vieira [1,2]

[1] Laboratório de Colisões Atómicas e Moleculares, CEFITEC, Departamento de Física
FCT-UNL, Quinta da Torre, 2829-516 Caparica, Portugal
[2] Centre of Molecular and Optical Sciences, Department of Physics and Astronomy
The Open University, Milton Keynes, MK 6AA, United Kingdom

The interaction of ionising radiation with living cells leads to the production of a large number of secondary electrons. These ballistic electrons, with energies of a few tenths of eV ($\leq$ 20 eV) can efficiently induce single and double strand breaks in supercoiled DNA [1]. Water is the surrounding medium in all living cells, and since it is a polar molecule it can easily trap electrons a process known as 'solvation'. Therefore it is extremely important to understand and assess the mechanism of these solvated electrons in the electron transfer process that can lead to DNA damage. The electronic state spectroscopy of water and its dissociation pathways are therefore essential in understanding radiation damage is living tissue. Accordingly as part of a wider programme of the study of electron and photon interactions with water we have investigated the electronic states spectroscopy of water.

The high resolution VUV photo-absorption cross section of water has been measured in the energy range 6 – 10.7 eV using synchrotron radiation at the ASTRID storage ring, ISA, University of Aarhus, Denmark, (Fig. 1). The present results are found to be in good agreement with previous data [2 - 4], but we have also observed new features in both the valence and Rydberg spectra. Fine structure observed in the photoabsorption spectra has been assigned to vibrational modes coupled to each observed Rydberg series and valence transitions. Further details will be given at the conference.

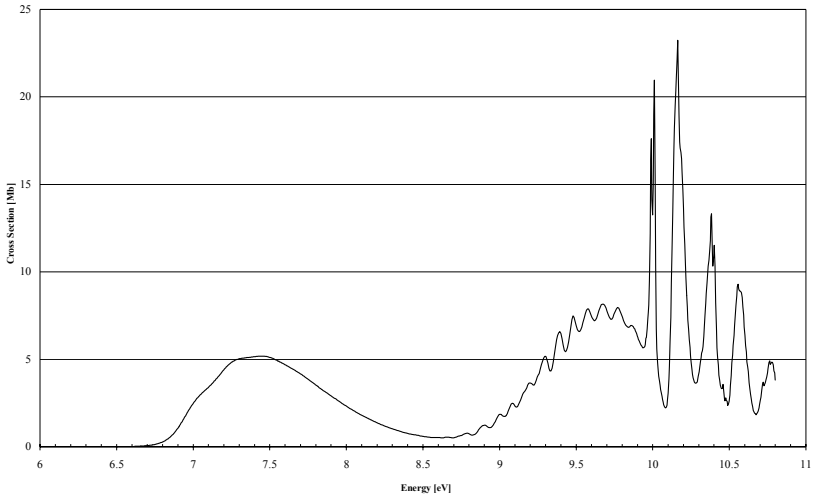


Fig. 1 – High resolution VUV photoabsorption spectrum of water.

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# Electron transfer in biomolecules by atomic scattering

V Kokhan [1], R Parafita [1], R Mota [1], N J Mason [2], G Garcia [3], M Maneira [1] and P Limão-Vieira [1,2]

[1] Laboratório de Colisões Atómicas e Moleculares, CEFITEC, Departamento de Física FCT-UNL, Quinta da Torre, 2829-516 Caparica, Portugal
[2] Centre of Molecular and Optical Sciences, Department of Physics and Astronomy The Open University, Milton Keynes, MK 6AA, United Kingdom
[3] Instituto de Matemáticas y Física Fundamental, Consejo Superior de Investigaciones Científicas, Serrano 113-bis, 28006 Madrid, Spain

Electron transfer reactions are a key process in transmission of electrons through the DNA helix and perhaps explains how SSB damage may lead to DSB and thence more complex damage Electron attachment by free electron interactions to the nucleic bases to determine both parent anion formation and subsequent fragmentation patterns is currently an active area of research, e.g., [1-3] since this plays an important role in the mechanisms of DNA and radiation damage. More recently, there has been particular interest in the investigation of the mechanisms that control the fragmentation of halouracils under electron impact. Some of these molecules [4] (e.g., 5-Chloro-uracil) are potential substitutes to be used in order to increase the sensitivity of DNA to ionising radiation and hence may be used in radiotherapy. However in the living cell electrons are not 'free' and other electron transfer processes may occur. Electron transfer in low energy atom-molecule collision is usually mediated by the crossing of the potential energy surfaces, K + AB (covalent) and K+ + AB- (ionic). Despite the fact that the ionic surface lies above the covalent at large atom-molecule distances, due to the Coulomb potential there is a crossing point at which both potential energy surfaces have the same value [5]. This crossing processes leads to the formation of both K+ and a molecular anion and allows access to states which are not accessible in free EA experiments [6]. In particular, states with a positive electron affinity can be formed, and the role of vibrational excitation of the parent neutral molecule can be studied [7]. In this case the electron donor is a potassium (K) atom and the electron acceptor molecule the biomolecule.

Using a crossed molecular beam technique we will investigate electron transfer processes in collisions of fast potassium atoms with DNA nucleotide bases and other relevant biomolecular targets such as sugars. We will investigate the formation of negative ions and thence model the parent anion state. Total partial cross sections will be obtained in an energy range from about a few eV up to several hundreds of eV. These experiments will allow us to probe whether such electron transfer processes behave similarly or differently from the single free electron attachment experiments yielding the same or different reaction products. This in turn will provide information on whether EA by free electrons is a correct model for electron transport in DNA or whether electron harpooning by bound electrons supplied in K - molecule scattering is a more appropriate model for electron transport under physiological conditions.

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# The electronic state spectroscopy of acetic studied by VUV synchrotron radiation, electron energy loss and He(I) photoelectron spectroscopy

R Mota [1], R Parafita [1], A Giuliani [2,3], M-J Hubin-Franskin [3], J Delwiche [4], D Duflot [5], J-P Flament [5], E Drage [6], P Cahillane [6], N J Mason [6] and P Limão-Vieira [1,6]

[1] Laboratório de Colisões Atómicas e Moleculares, CEFITEC, Departamento de Física FCT-UNL, Quinta da Torre, 2829-516 Caparica, Portugal
[2] ICSN – CNRS, Avenue de la Terrasse, Bat. 27, 91198 Gif-sur-Yvette, France
Institut de Chimie-Bât. B6C, B-4000 Liège, Belgium
[3] Laboratoire de Spectrsocopie d'Electrons Diffusés, Université de Liège, Institut de Chimie-Bât. B6C, B-4000 Liège, Belgium
[4] Laboratoire de Thermodynamique et Spectroscopie, Université de Liège, Institut de Chimie-Bât. B6C, B-4000 Liège, Belgium
Physique des Lasers, Atomes et Molécules, UMR CNRS 8523
[5] Centre d'Etudes et de Recherches Lasers et Applications, Université des Sciences et Technologies de Lille, F-59655 Villeneuve d'Ascq Cédex, France
[6] Centre of Molecular and Optical Sciences, Department of Physics and Astronomy The Open University, Milton Keynes, MK 6AA, United Kingdom

Acetic acid (CH3COOH), commonly known as vinegar, is produced in the human body as a result of alcohol synthesis after the consumption of alcoholic beverages. It also plays an important role in the metabolism processes of most forms of life and results naturally from the action of certain bacteria in foods or liquids containing sugars or ethanol. Despite the fact that, after formic acid (HCOOH), acetic acid is the second simplest organic acid, and therefore an important component of biological molecules, its spectroscopy remains largely unknown.

We have conducted a series of experiments on acetic acid. In this report we present the electronic state spectroscopy of CH3COOH as studied by VUV photo-absorption measurements in the energy range 3.5 – 11.0 eV. The high-resolution photon beam (~ 0.075 nm) derived form a synchrotron source (ASTRID In aarhus Denmark) has allowed a detailed analysis of the vibrational progressions to be made and new assignments of the Rydberg series to be determined , where some new series are observed for the first time These results are compared with electron energy loss spectra (EELS) collected at an incident energy of 100 eV are analysed post-interaction at a scattering angle ~ 0° in the energy loss range. A high resolution He(I) photoelectron spectrum has been also recorded [2].Full details will be given at the meeting.

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**Effect of batch process solar disinfection (SODIS) on the survival of *Cryptosporidium parvum* oocysts in drinking water**

K.G. McGuigan [1], S.C.Kehoe[2], F. Méndez-Hermida [3], E. Ares-Mazás [3].

[1,2]Depts. of Physiology & Medical Physics(1) and Surgery(2), RCSI
[3]Dept. of Microbiology, University of Santiago de Compostela, Spain

Batch – process solar disinfection (SODIS) is a technique for improving the quality of biologically contaminated water. It involves the storage of contaminated drinking water in transparent containers that are placed in direct sunlight for a minimum of 6 h. This study investigated the efficacy of SODIS for the inactivation of *Cryptosporidium. parvum* oocysts in experimentally infected water. *C. parvum* oocyst suspensions were exposed to the light generated by a solar simulator for different exposure times at a constant temperature of 40º C. Viability assays were performed using DAPI/PI fluorogenic dyes and excystation techniques. Infectivity tests were carried out using a Swiss CD-1 suckling mice infectivity model. Exposure times $\geq$ 10 h (total optical doses > 30kJ) rendered oocysts non-infective. We observed that temperature alone does not influence oocyst infectivity. This work confirms that SODIS can be used for the disinfection of drinking water contaminated with *C. parvum* oocysts. It is shown to be an appropriate alternative technology for water disinfection in developed and developing countries and as an emergency intervention against waterborne disease in areas effected by natural disaster [1].

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# Absolute energy and angle dependent cross sections for elastic electron scattering by tetrahydrofuran molecule

A. R. Milosavljevic[1], A. Giuliani[2], D. Ševiş[1], M.-J. Hubin-Franskin[2] and B. P. Marinkoviş[1]

[1] Institute of Physics, Pregrevica 118, 11080 Belgrade, Serbia and Montenegro
[2] Laboratoire de Spectroscopie d'Electrons Diffusés, Université de Liège, Institut de Chimie, Bâtiment B6c, B-4000 Liège, Belgium

We report absolute cross sections for elastic scattering of electrons by tetrahydrofuran (THF) molecule (C4H8O), in the energy range from 10 eV to 300 eV and the angular range from 10o to 110o. The investigation of THF, which is the DNA backbone sugar-like analogue, gives possibilities for better comprehending the effects of secondary electrons, induced by ionizing radiation, on the DNA sugar chain. In this context, some results for THF, considering vibrational excitation and dissociative electron attachment, for the impact energies up to about 30 eV, have been reported recently [1], [2]. However, according to our knowledge, there is no published data for elastic electron scattering by THF. Therefore, obtaining a set of absolute cross sections for elastic electron-THF scattering, in a large energy domain, is of interest for radiation biology and modeling of radiation damage processes, as well.

The experimental results that we report here have been obtained on two different apparatus, one placed in Liege and the other in Belgrade. The former one includes a monochromator and an energy analyzer, both of 150o hemispherical electrostatic type, and is characterized by a high energy resolution of about 45 meV. On this apparatus, the absolute differential cross sections (DCSs) for elastic electron scattering by THF have been obtained according to measurement of the ratio of the elastically scattered intensity of THF to that of N2. The other apparatus, placed in Belgrade, includes an electron gun and double cylindrical mirror energy analyzer, fitted with four-electrode zoom lens. The lowest energy resolution of about 0.5 eV is limited by thermal spread of incident electrons. However, on this apparatus the relative DCSs can be measured as a function of both scattering angle and incident electron energy and, hence, the absolute normalized, independent data set can be obtained according to a single absolute DCS value in the overlapping region. The angle dependent absolute DCSs at two overlapping incident energies are presented in figure 1(a,b). Also, a relative energy dependent DCS at 32o is presented in figure1.

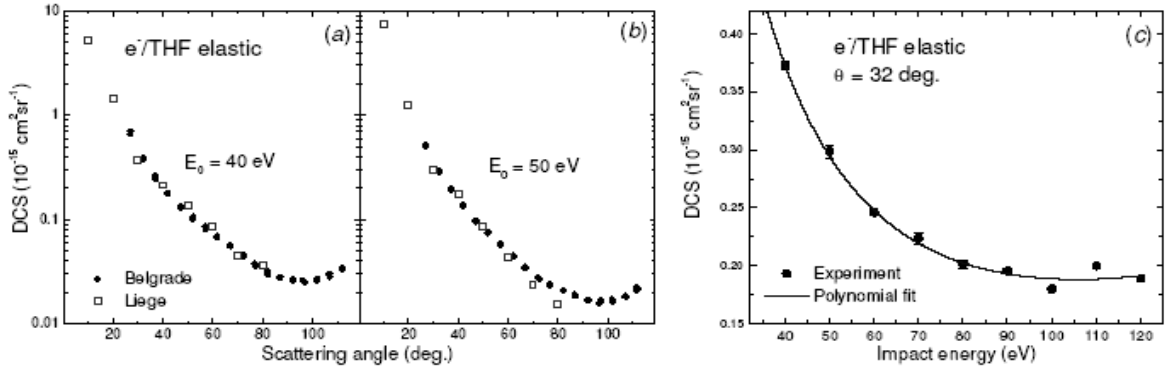


Figure 1. (a,b) Absolute angle dependent DCSs; (c) Relative energy dependent DCS.

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# The assignment of dissociative electron attachment bands in compounds containing hydroxyl and amino groups

T. Skalický[1,2] and M. Allan[2]

Department of Chemistry, University of Fribourg, Chemin du Musée 9, 1700 Fribourg, Switzerland
Institute of Chemistry, Physical and Theoretical Chemistry, Free University of Berlin, Takustr. 3, 14195 Berlin, Germany

Dissociative electron attachment (DEA) spectra were recorded for methanol, phenol, diethylamine, tetramethylhydrazine, piperazine, pyrrole and N,N-dimethylaniline. Comparison with He I photoelectron spectra permitted the assignment of virtually all DEA bands in the saturated compounds to core excited Feshbach resonances with double occupation of Rydberg-like orbitals and various Koopmans' states of the positive ion as a core. These resonances shift to lower energies with alkyl substitution, in contrast to the shape resonances, and are found at surprisingly low energies in the amines. The DEA spectra in the unsaturated compounds show no or only weak evidence for the Rydberg-type Feshbach resonances. It is proposed that DEA in saturated polyatomic molecules containing hydroxyl and amino groups is in general dominated by this type of resonances.

The work on methanol and tetramethylhydrazine is shown in figure 1 as an example.

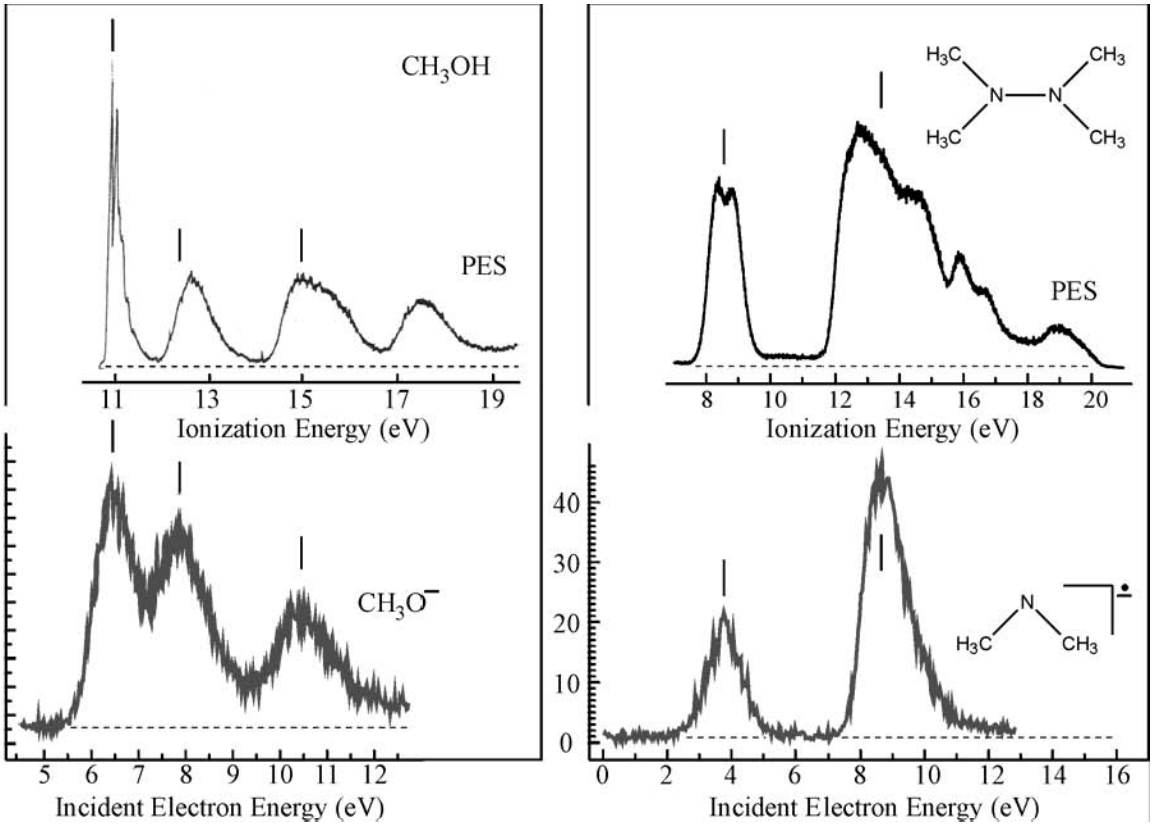


**Fig. 1.** Comparison of the dissociative electron attachment spectra of methanol and tetramethylhydrazine and their photoelectron spectra (PES). The DEA bands and PES bands are shifted by ~ 4.5 eV. The photoelectron spectrum of methanol is taken from the work of Kimura.[1]

# Imaging of UV-induced damage in DNA

M. Śmiałek[a], N. Mason[a], D.Jaksch[a], S. Moore[a],
M. Jasionowski[b], J. Rak[b]

[a]Department of Physics and Astronomy, The Open University, Walton Hall, Milton Keynes, Buckinghamshire, Great Britain, MK7 6AA
[b]Department of Chemistry, University of Gdańsk, Sobieskiego 18, 80-952 Gdańsk, Poland

Development of new imaging instruments such as the Atomic Force Microscope (AFM) allows scientists to image object on the micro and nanoscale with unparallel resolution [1]. Using the tapping mode [2], AFM can be widely used for imaging soft, biological samples, such as DNA. Previous investigations have shown that using this methodology, we are able not only see DNA itself, but also a damage caused by external factors [3, 4]. In our investigations we are trying to show, how UV irradiation can affect the inner structure of DNA double helix, namely if it is possible to induce single- or even double strand breaks. Some interesting studies [5] have already been made in this area, but it is still important to ensure that obtained that way results are reproducible.

We are investigating the behavior of pBR322 plasmid DNA in solution with water. To quantify the difference in volume of unaffected DNA and DNA that has been damaged during irradiation, after exposing them to UV light we place the samples on agarose gels and using the method of electrophoresis to identify single and double strand breaks. However, agarose gel electrophoresis is a destructive method that does not allow the sample to be studied concurrently, using AFM we hope to be able to study successive irradiations of the same DNA sample and hence look at aggregated damage. AFM may also allow us to characterize the size of strand fragments after irradiation. When using AFM analysis we place our plasmid samples on non-treated mica surface using 1 mM MgCl2 solution.

Initial results have shown that we can detect UV light induced damage Further results and discussion of future work will be presented at the conference, including a discussion of how the technique may be developed to investigate electron and ion induced DNA damage.

**Acknowledgements:** This work was supported by the UK Research Councils EPSRC and MRC and the British Polish Research Partnership Programme (J.R. and N.M.; grant no. WAR/341/257

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# Low-Energy Electron Damage to DNA Oligonucleotides

T. Solomun and E. Illenberger

Free University Berlin, Institute of Chemistry, Takustrasse 3, D-14195 Berlin, Germany.

It has been shown recently [1] that damage to DNA oligonucleotides by impinging very low energy (< 3eV) electrons can be detected and analysed through the subsequent interaction with the complementary strand. The DNA damage is a result of a dissociative electron attachment at energies below the threshold for electronic excitations. We have extended the initial feasibility study on hetero G-T oligonucleotides to a more quantitative (fluorescence) analyses and assessment of the dependence of the damage to T25 oligonucleotides end-tethered on gold surface as a function of electron energy and dosage.

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# Fragmentation of $CH_4$ and $H_2O$ molecules following 800 keV $He^+$ impact: First results

B. Sulik[1], T. Ricsóka[1], F. Gáll[1], and N. Stolterfoht[2]

[1]Institute of Nuclear Research of the Hungarian Academy of Sciences (ATOMKI), Debrecen, Hungary
[2]Hahn-Meitner Institute Berlin, Glienickerstr. 100, D-14109 Berlin, Germany

The energy distributions of fragments produced in 800 keV $He^+$ + $H_2O$, and $He^+$ + $CH_4$ collisions have been measured at the beamline of a Van de Graaff electrostatic accelerator in ATOMKI, Debrecen. The data are compared to those, measured earlier for $Ne^{q+}$ + $H_2O$ collisions at much lower projectile energies in HMI, Berlin [1].

In the present work we study the low recoil-ion energy group, which extends up to ~ 45 eV, and corresponds to Coulomb explosion (CE) of the ionized target ($H_2O$). The ionization mechanisms are direct ionization and excitation for the present ATOMKI data, and electron capture for the HMI data.

Coulomb explosion is a common mechanism for fragmentation in both fast and slow ion impact. In the case of water target, the characteristic energies for the fragment peaks are the same for the HMI and the ATOMKI data.

The spectra of ion fragments from methan is rather different, especially for the yields of the different charge states. For fast collisions, we are going to study the details of the vacancy production mechanisms.

This work has been supposted by the COST Action P9, and by the Hungarian OTKA Fund (T045905)

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# Electron emission near the Bragg peak: the contribution of fast electrons accelerated by multiple electron scattering

B. Sulik[1], K. Tőkési[1] and N. Stolterfoht[2]

[1]Institute of Nuclear Research of the Hungarian Academy of Sciences (ATOMKI), Debrecen, Hungary
[2]Hahn-Meitner Institute Berlin, Glienickerstr. 100, D-14109 Berlin, Germany

Swift ions, when decelerating in biological tissues, liberate many electrons along their trajectories. These electrons represent a secondary radiation, which has the longest range among charged particles. There are various mechanisms, how these electrons can interact with the molecules of the tissue. The angular and energy distribution of the emitted electrons strongly varies along the ion-path as its velocity decreases down to zero. Accurate knowledge of the amount and distribution of the emitted electrons is especially important in the region of the Bragg peak, at the end of the ion trajectory, where the largest part of the ion-energy is deposited.

In the present work, we demonstrate that a large amount of high-energy (between a few tens and a few hundreds eV) electrons can be emitted near to the Bragg peak, i.e., when the ion has been decelerated down to a few keV total kinetic energy. The mechanism of fast electron emission is the so-called Fermi-shuttle acceleration [1,2], where the electron is scattered forward and backward by the incoming heavy projectile ion and the target core before being ejected. Due to the repeated collisions, the electron can be accelerated to high energies. In recent works [3,4], evidence has been provided for double (projectile-target, P-T), triple (P-T-P) and quadruple (P-T-P-T) scattering sequences in ion-atom collisions. Our latest measurements and the corresponding CTMC calculations have shown that accelerating multiple electron scattering can even dominate electron emission for slow ion impact, providing a large amount of unexpectedly high-energy electrons.

The surrounding of the Bragg peak, i.e., the region where most of the ion energy is deposited, is strongly localized for heavy ions. For radiation therapies it is vitally important to know, how large part of the deposited energy will escape, and damage a larger surrounding of the target area.

Supported by the Hungarian OTKA Fund (T045905)

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# Radiobiological Yeast *Saccharomyces Cerevisiae* cell array experiments using SAM technology

Š. Vaitekonis[1)], R. Plukienė [1)], A. Plukis[1)], V. Remeikis[1)] and D. Čitavičius [2)]

(1) Institute of Physics, Vilnius, Lithuania
(2) Vilnius University, Faculty of Natural Sciences

The application of SAM (self-assembled monolayer) for yeast *Saccharomyces Cerevisiae* cells array irradiation is investigated. SAM technique [1] is chosen in order to irradiate the exact number of yeast cells (cells array) in thick layer of 10 μm (yeast cell dimensions) and for irradiation of several cells possibilities. Deposition of mutant yeast strains cells of Peterhoff genetic line which possesses *Ras* proteins homologous to higher eukaryotes [2] is performed.

Radiobiological covers yeast cells synchronization, deposition on SAM, irradiation using gamma or X-rays, cell survival analysis and flow cytometric cell cycle progression analysis. Test experiments with two irradiation geometries were performed – direct irradiation of the cell arrays by X-rays and the specific back irradiation geometry when photons interacts with substratum materials on which SAM is assembled. In this case energy transfer to yeast cells is performed via secondary electrons produced in a photon interaction due to Compton scattering and Bremstrallung process. The experimental scheme, gamma/secondary electrons energy distribution and radiation dose are modeled using MCNPX code [3]. Survival of the cells after irradiation and progression during cell cycle were criterions of yeast sensitivity to radiation [4].

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# Interactions of electrons with biomolecules

M. Vinodkumar[1,3], K. N. Joshipura[2], Nigel Mason[3]

[1]V. P. & R. P. T. P. Science College, Vallabh Vidyanagar, Gujarat, 388 120, India
[2]Department of Physics, Sardar Patel University, Vallabh Vidyanagr, 388 120, India
[3]Department of Physics and Astronomy, The Open University, Milton Keynes, MK7 6AA

One of the goals of radiation biology is to develop a model of how ionizing radiation interacts with living tissues, from the initial energy deposition event at the molecular level, through to the longer term consequences for the whole organism [1]. It is therefore necessary to study the ionisation of biomolecules by both the primary radiation and secondary electrons induced in the initial ionizing events. The study of electron induced ionisation for simple gas phase molecules is a well established field of atomic and molecular physics, with well defined experimental techniques capable of providing accurate cross sections (to within a few percent). However in biology there are many molecular systems that can not be prepared for experiment ( e.g short lived radicals of molecules that can not be easily prepared in the gas phase- DNA for example !) for such targets ionisation cross sections must be evaluated using theoretical methods.

Theoretical track structure modelling is used to stimulate the distinctive patterns of ionizations produced by wide range of ionizing radiations. Such methods show us that penetrating radiations produce a significant number of nanometre-sized clusters of ionization at the low energy track-ends of secondary electrons. Similarly, ions produce an abundance of clustered ionization along the path of the particle track both by the ions themselves and low energy secondary electrons. Such clusters can induce complex strand breaks in DNA, which are less easily repaired than the predominantly simple breaks produced by energetic electrons. The low energy electrons therefore have an important role in determining the overall radiobiological effect of the ionizing radiation and the mechanisms by which it may damage DNA.

We have developed a simple hybrid theory Modified Single centre Additivity Rule (MSCAR) to calculate electron impact scattering cross sections from different atomic and molecular species. Our calculations are carried out using a Complex Optical Potential(COP) formalism. The COP consists of real and imaginary model potentials which are used to derive the total cross sections[2,3]. The total ionization cross sections are obtained by DM formalism[4]. The study has been carried out for simple biomolecules like formaldehyde, formamide, etc. The detailed results will be presented in the conference.

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# DNA mediated charge migration

Marian Wolszczak and Malgorzata Steblecka

Institute of Applied Radiation Chemistry, Technical University of Lodz
Wroblewskiego 15, 93-590 Lodz, Poland

For many years both experiment [1-3] and theory [4-5] have been applied to determine whether the DNA π – stack facilitates charge transport over extended molecular distances. Despite the long debate concerning process of electron transfer along helical DNA duplex the electronic properties remain highly controversial. The process is important because charge migration through DNA plays crucial role in mutagenesis and carcinogenesis. From a practical perspective, understanding of charge migration process in DNA is important in the development of nanoscale electronic devices [6].

In this presentation we report on the pulse radiolysis studies under conditions where the electron is captured by DNA bases and subsequent electron transfer to the intercalator is observed. The main factors influencing such transfer will be analyzed, namely: the coupling of the intercalator into the base pairs stack and the driving force for electron scavenging reaction.

Photoinduced electron transfer reactions between photoexcited intercalator and acceptor are compared in water solution and DNA. Luminescence and transient absorption results indicate electron tunneling is restricted to less than five base pairs. Special attention will be paid to the elucidation the role of the ionic strength of the solution on the rate constant of the electron transfer process. Using the steady-state and time resolved photolysis techniques, the values of the bimolecular quenching constant for the reaction of 9-aminomethylanthracene cation with methylviologen in aqueous solutions have been determined for various concentrations (0 - 3 mol $dm^{-3}$) and types (LiCl, $NaClO_4$, NaCl, $NaBF_4$ and $CaCl_2$) of the electrolyte. For the selected systems the influence of temperature on quenching constant has been determined experimentally yielding the activation energy and the solvent reorganization energy of the electron transfer process.

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# Index

# Addresses and e-mails of participants


1. Ms. Fresia Alvarado
   KVI Atomic Physics, Zernikelaan 25
   9747AA Groningen, The Netherlands
   alvarado@kvi.nl

2. Prof. Lars Henrik Andersen
   University of Aarhus,
   8000 C Aarhus, Denmark
   lha@phys.au.dk

3. Dr. Marie-Christine Bacchus
   Université Claude Bernard Lyon I, 43, Bd
   11 Novembre 1918
   69622 Villeurbanne Cedex, France
   bacchus@lasim.univ-lyon1.fr

4. Dr. Woon Yong Baek
   Physikalisch-Technische Bundesanstalt,
   Bundesallee 100
   38116 Braunschweig, Germany
   Woonyong.Baek@ptb.de

5. Mr. Ilko Bald
   FU Berlin-Institut für Chemie, Takustrasse 3
   14195 Berlin, Germany
   bald@chemie.fu-berlin.de

6. Dr. Martin Beyer
   Department of Chemistry 2, Technical
   University Munich
   85747 Munich, Germany
   martin.beyer@ch.tum.de

7. Prof. Krzysztof Bobrowski
   Institute of Nuclear Chemistry and
   Technology, Dorodna 16
   03-195 Warszawa, Poland
   kris@orange.ichtj.waw.pl

8. Ms Maria Boyle
   RCSI, 123 St Stephen's Green
   2 Dublin, Ireland marboyle@rcsi.ie

9. Prof. Steen Brondsted Nielsen
   University of Aarhus,
   8000 C Aarhus, Denmark
   sbn@phys.au.dk

10. Ms. Emilie Cauët
    Université Libre de Bruxelles,
    50 av. F. D. Roosevelt,CP160/09
    1050 Bruxelles, Belgium
    ecauet@ulb.ac.be

11. Prof. Henrik Cederquist
    Stockholm University, Department of
    Physics
    106 91 Stockholm, Sweden
    cederquist@physto.se

12. Dr. Jean-Yves Chesnel
    CIRIL-EnsiCaen,
    6, Boulevard Maréchal Juin
    14050 Caen Cedex 04, France
    jean-yves.chesnel@ensicaen.fr

13. Prof. Wolfgang Domcke
    Department of Chemistry, Technical
    University Munich
    85747 Munich, Germany
    Wolfgang.Domcke@ch.tum.de

14. Dr. Michel Farizon
    IPNL, 4, Rue Enrico Fermi
    69622 Villeurbanne, France
    mfarizon@ipnl.in2p3.fr

15. Dr. David Field
    University of Aarhus,
    Ny Munkegade
    8000 C Aarhus, Denmark
    dfield@phys.au.dk

16. Prof. Melvyn Folkard
    Gray Cancer Institute, Mount Vernon
    Hospital Northwood,
    Middlesex HA6 2JR, UK
    folkard@gci.ac.uk

17. Dr. Werner Friedland
    Institut für Strahlenschutz GSF,
    Ingolstädter Landstr. 1
    85764 Neuherberg, Germany
    friedland@gsf.de

18. Prof. Bojidar Galutzov
Sofia University, 8 Dragan Tzankov blvd
1164 Sofia, Bulgaria
galutzov@biofac.uni-sofia.bg

19. Prof. Gustavo Garcia Gomez Tejedor
Instituto de Mathemáticas y Física
Fundamental, C/Serrano 121
28006 Madrid, Spain
g.garcia@imaff.cfmac.csic.es

20. Dr. Yann A. Gauduel
Laboratoire d'Optique Appliquée, Ecole
Polytechnique Palaiseau
Paris, France
Yann.Gauduel@ensta.fr

21. Prof. Franco A. Gianturco
CASPUR, Via dei Tizii, 6/b
00185 Roma, Italy
fa.gianturco@caspur.it

22. Mr. Sascha Gohlke
FU Berlin-Institut für Chemie, Takustrasse 3
14195 Berlin, Germany
sascha.gohlke@chemie.fu-berlin.de

23. Ms. Monika Golebiowska
University of Gdansk, Sobieskiego 18/19
80-952 Gdansk, Poland
monikag@chemik.chem.univ.gda.pl

24. Dr. Leticia González
FU Berlin-Institut für Chemie, Takustrasse 3
14195 Berlin, Germany
leti@chemie.fu-berlin.de

25. Dr. Agustin Grau Carles
IMAFF/CSIC, C/ Serrano, 113b
28006 Madrid, Spain
agrau@imaff.cfmac.csic.es

26. Dr. Agustin Grau-Malonda
CIEMAT, Avda. Complutense 22
28040 Madrid, Spain
agustin.grau@ciemat.es

27. Dr. Bernd Grosswendt
Physikalisch-Technische Bundesanstalt,
Bundesallee 100
38116 Braunschweig, Germany
bernd.grosswendt@ptb.de

28. Mr. Rolf Hellhammer
Hahn-Meitner Institut, Glienickerstrasse 100
14109 Berlin, Germany
hellhammer@hmi.de

29. Dr. Mark Hill
MRC Radiation & Genome Stability Unit,
Becquerel Av
OX11 0RD Harwell, Oxfordshire, United
Kingdom
m.hill@har.mrc.ac.uk

30. Prof. Ronnie Hoekstra
KVI Atomic Physics, Zernikelaan 25
9747AA Groningen, The Netherlands
hoekstra@kvi.nl

31. Prof. Bernd A. Huber
CIRIL/GANIL, Rue Claude Bloch
14070 Caen, France
huber@ganil.fr

32. Dr. Adam Hunniford
Queen's University, University Road
BT7 1NN Belfast, United Kingdom
c.a.hunniford@qub.ac.uk

33. Prof. Preben Hvelplund
Institute of Physics, University of Aarhus
8000 Aarhus C, Denmark
hvelplun@phys.au.dk

34. Prof. Eugen Illenberger
FU Berlin-Institut für Chemie, Takustrasse 3
14195 Berlin, Germany
iln@chemie.fu-berlin.de

35. Dr. Marek Jasionowski
University of Gdansk, Sobieskiego18
80-952 Gdansk, Poland
marekj@chem.univ.gda.pl

36. Dr. Sandrine Lacombe
Université Paris Sud 11
91405 Orsay, France
sandrinelacombe@aol.com

37. Dr. Arnaud Le Padellec
UPS-Toulouse IIIR1b4,
118 route de Narbonne
31062 Toulouse, France
arnaud.lepadellec@irsamc.ups-tlse.fr

38. Mr. Sébastien Legendre
CIRIL-Ganil,
Avenue H. Becquerel B.P. 5133
14070 Caen cedex 05, France
legendre@ganil.fr

39. Prof. Jacques Liévin
Université Libre de Bruxelles,
50 av F.D. Roosevelt CP160/09
1050 Bruxelles, Belgium
jlievin@ulb.ac.be

40. Dr. Paulo Limao-Vieira
New University of Lisbon, Quinta da Torre
2829-516 Caparica, Portugal
plimaovieira@fct.unl.pt

41. Dr. Bratislav Marinkovic
Institute of Physics Belgrade,
Pregrevica 118
11080 Belgrade, Serbia and Montenegro
bratislav.marinkovic@phy.bg.ac.yu

42. Prof. Nigel Mason
The Open University,
Walton Hall
MK76AA Milton Keynes, United Kingdom
n.j.mason@open.ac.uk

43. Dr. Kevin McGuigan
RCSI, 123 St Stephen's Green
2 Dublin, Ireland
kmcguigan@rcsi.ie

44. Mr. Aleksandar Milosavljevic
Institute of Physics Belgrade,
Pregrevica 118
11080 Belgrade, Serbia and Montenegro
vraz@phy.bg.ac.yu

45. Ms. Raquel Mota
Faculdade de Ciencias e Tecnologia, Quinta de Torre
2829-516 Caparica, Portugal
raquelmota@sapo.pt

46. Prof. Andrea Ottolenghi
Dipartimento di Fisica Nucleare e Teorica,
Università degli Studi di Pavia, Via Bassi 6
27100 Milan,Italy
Andrea.Ottolenghi@pv.infn.it

47. Prof. Herwig Paretzke
Institut für Strahlenschutz GSF,
Ingolstädter Landstr. 1
85764 Neuherberg, Germany
paretzke@gsf.de

48. Dr. Rita Plukiene
Institute of Physics, Savanoriu ave. 231
02300 Vilnius, Lithuania
rita@ar.fi.lt

49. Dr. Arturas Plukis
Institute of Physics, Savanoriu ave. 231
02300 Vilnius, Lithuania
arturas@ar.fi.lt

50. Dr. Kevin Prise
Gray Cancer Institute, Mount Vernon Hospital Northwood
WD3 3SS Northwood, UK
prise@gci.ac.uk

51. Dr. Stanislaw Pszona
Soltan Institute for Nuclear Research
05-400 Otwok/Swierk, Poland
pszona@ipj.gov.pl

52. Dr. Sylwia Ptasinska
Institut für Ionenphysik, Universität Innsbruck, Technikerstr. 25
6020 Insbruck, Austria
sylwia.ptasinska@uibk.ac.at

53. Prof. John Sabin
University of Southern Denmark,
Campusvej 55
5230 Odense, Denmark
sabin@qtp.ufl.edu

54. Dr. Evelyne Sage
CRNS and Institute Curie, 26 rue d'Ulm
75248 Paris cedex 05, France
Evelyne.Sage@curie.u-psud.fr

55. Dr. Egon Schedler
SNI, 35, Rue des Alliés
38100 Grenoble, France
sni.schedler@laposte.net

56. Prof. Paul Scheier
Institut für Ionenphysik, Universität
Insbruck, Technikerstr. 25
6020 Insbruck, Austria
paul.scheier@uibk.ac.at

57. Dr. Thomas Schlathölter
Kernfysisch-Versneller Instituut,
Zernikelaan 25
9747 AA Groningen, The Netherland
Tschlat@KVI.nl

58. Prof. Luis Serrano-Andrés
Instituto de Ciencia Molecular, Universitat
de València, Dr. Moliner 50
46100 Burjassot (Valencia), Spain
Luis.Serrano@uv.es

59. Dr. Tomas Skalicky
FU Berlin-Institut für Chemie, Takustrasse 3
14195 Berlin, Germany
skalicky@chemie.fu-berlin.de

60. Ms. Malgorzata Smialek
The Open University, Walton Hall
MK76AA Milton Keynes, United Kingdom
m.a.smialek@open.ac.uk

61. Dr. Przemek Sobocinski
Hahn-Meitner Institut, Glienickerstrasse 100
14109 Berlin, Germany
sobocinski@hmi.de

62. Dr. Tihomir Solomun
FU Berlin, Takustrasse 3
14195 Berlin, Germany
solomun@chemie.fu-berlin.de

63. Prof. Clemens von Sonntag
Max Planck Institut Mühlheim (Ruhr),
Bleichstr. 16
45468 Mühlheim, Germany
Clemens@vonsonntag.de

64. Dr. Melanie Spotheim-Maurizot
Centre de Biophysique Moleculaire,
Rue C. Sadron
45071 Orléans, France
spotheim@hermes.cnrs-orleans.fr

65. Ms. Viktorie Štísová
Nuclear Physics Institute, Radiation
Dosimetry Department
180 86 Prague 8, Czech Republic
stisova@ujf.cas.cz

66. Prof. Nikolaus Stolterfoht
Hahn-Meitner Institut, Glienickerstrasse 100
14109 Berlin, Germany
stolterfoht@hmi.de

67. Dr. Béla Sulik
Institute of Nuclear Research (ATOMKI),
Bem tér 18/c
4026 Debrecen, Hungary
sulik@atomki.hu

68. Dr.Yvette-Suzanne Tergiman
Université Claude Bernard Lyon I,
43, Bd 11 Novembre 1918
69622 Villeurbanne Cedex, France
tergiman@lasim.univ-lyon1.fr

69. Mr. Sarunas Vaitekonis
Institute of physics, Savanoriu ave. 231
02300 Vilnius, Lithuania
sarunas@ar.fi.lt

70. Dr. Minaxi Vinodkumar Pothodi Chackra
The Open University, Walton Hall
MK76AA Milton Keynes, United Kingdom
minaxivinod@yahoo.co.in

71. Dr. Amalia Williart
UNED, Senda del Rey nº 9
28040 Madrid, Spain
awilliart@ccia.uned.es

72. Dr. Marian Wolszczak
Technical University, Wroblewskiego 15
93-590 Lodz, Poland
marianwo@mitr.p.lodz.pl